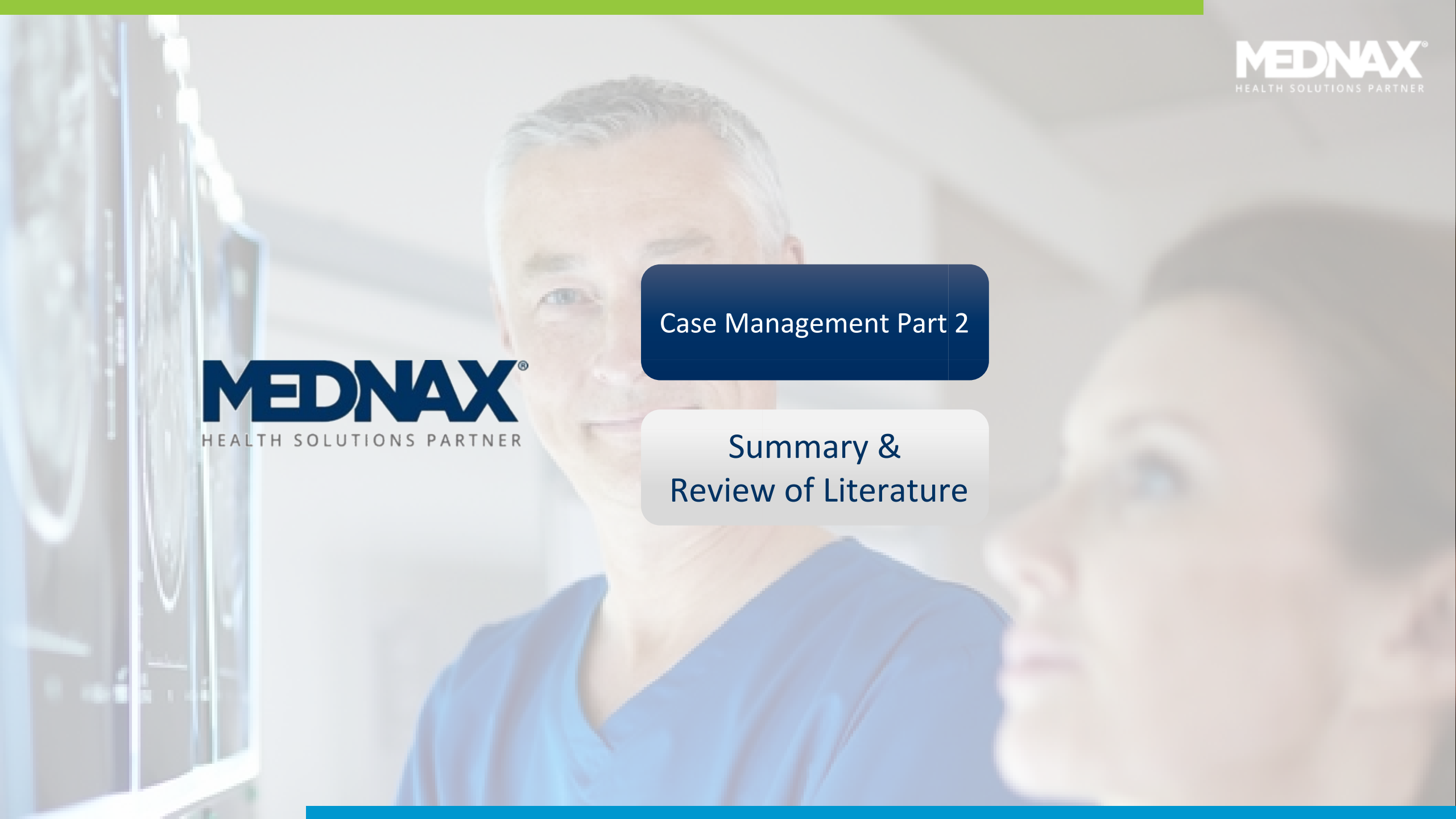


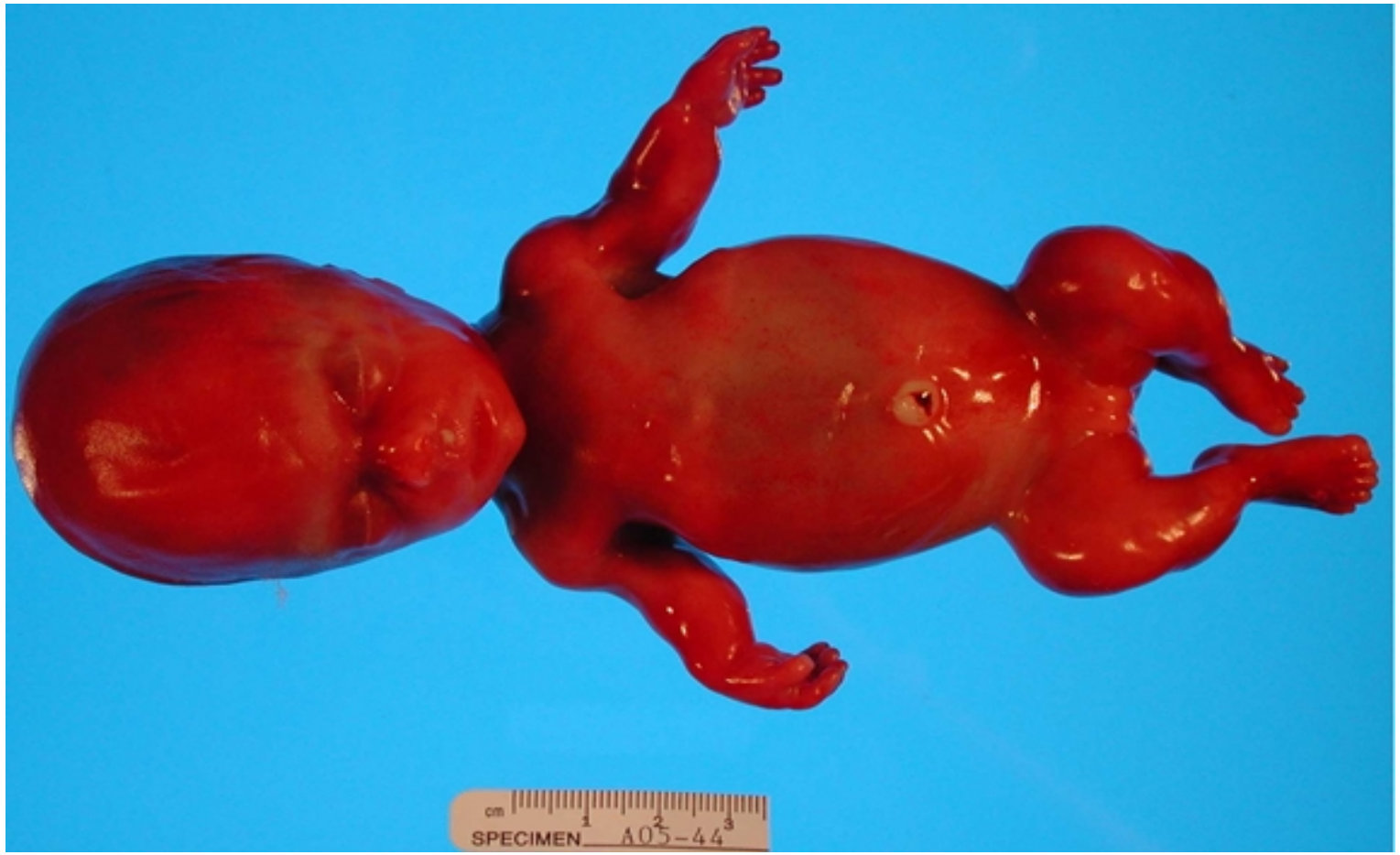
Case Management Part 2

Summary & Review of Literature

Part 2 – Case Management

Given the ultrasound findings of severe rhizomelia, bell-shaped chest, normal heart that appears abnormally large within the small chest, and “telephone-receiver” appearance to the femur, the patient was counseled about the probability of a lethal skeletal abnormality. After consideration, at 22 weeks’ gestation, she opted for termination of the pregnancy. An autopsy confirmed the above findings, and was consistent with a diagnosis of ‘Thanatophoric dysplasia Type I’, a genetic skeletal disorder (see image 7).

Image 7 – Thanatophoric dysplasia Type I




MEDNAX
HEALTH SOLUTIONS PARTNER
Summary &
Review of Literature

Summary & Review of Literature

Thanatophoric dysplasia is the most common of the lethal short-limb dwarfism syndromes. The name derives from the Greek word “Thanatophoros,” which means “death bearing.” Most neonates with this disorder die within the first hours of life primarily due to pulmonary hypoplasia. There are, however, isolated case reports of survival of severely developmentally delayed children into the pre-teen years, and a report of a moderately developmentally delayed mosaic patient surviving into her 50s. Thanatophoric dysplasia occurs in about 1/20,000 live births. There are two types, Type I and Type II. The former is characterized by bowed femurs and the latter by cloverleaf skull deformity, although either type is occasionally associated with both features. Our patient, who displayed bowed femurs and did not have a cloverleaf skull deformity, is a classic Type I. TD1 and TD2 are autosomal dominant disorders and as such virtually all cases are due to spontaneous mutations. These mutations are in the fibroblast growth factor receptor 3 (FGFR3) gene. TD has a paternal bias in mutation origin because of DNA copy errors during male gametogenesis, and has a paternal age effect.

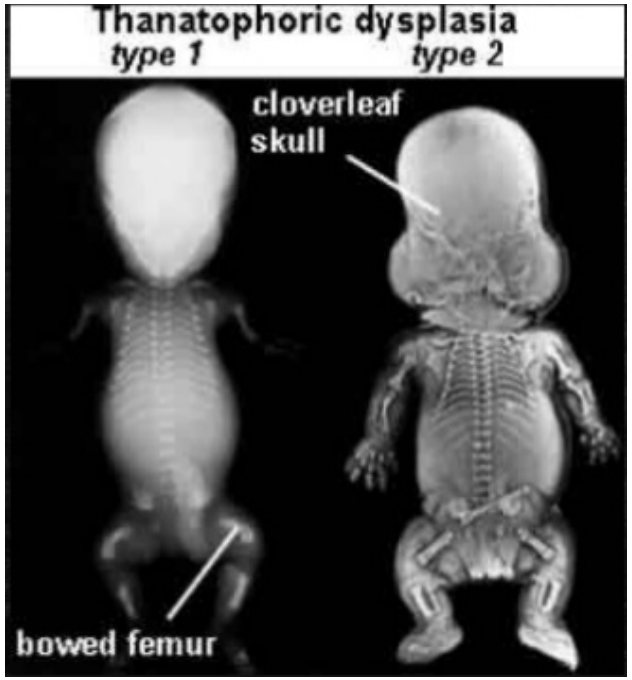
Summary & Review of Literature

Another revealing sign of this type of dysplasia is hypoplastic thorax. This gives rise to specific findings, depicted in our patient, such as a structurally normal heart that appears large (taking up more than 60% of the chest cavity) within the small thorax and a bell-shaped appearance to the thorax/abdomen. Other ultrasonographic findings that raise suspicion about thanatophoric dysplasia include rhizomelia (proximal bone shortening, especially with characteristic “telephone-receiver” bowing), intrauterine growth retardation, well-ossified spine and skull, platyspondyly, ventriculomegaly, short ribs, polyhydramnios, and macrocephaly.

In contrast TD2 presents with micromelia but with long-bones (femurs) that are straight and not as short as those seen in TD type 1, platyspondyly of the vertebrae, narrow thorax, and a cloverleaf (trilobed) skull. Distinctive facial features include macrocephaly, frontal bossing, low nasal bridge, large anterior fontanel and proptosis. Polyhydramnios is common. Neonates usually die shortly after birth due to respiratory insufficiency and/or spinal cord/brain stem compression.

Summary & Review of Literature

Conditions with overlapping findings should be in the differential diagnosis, such as achondroplasia, the achondrogenesis, osteogenesis imperfecta Type II, short rib-polydactyly syndromes, campomelic dysplasia, rhizomelic chondrodysplasia punctata, platyspondylic lethal skeletal dysplasia, and dyssegmental dysplasia.



Summary & Review of Literature

The prognosis is extremely poor; as noted above, there are no reports of intact survivorship. Obviously, early prenatal detection is key when considering options for a lethal condition. Ultrasound is excellent for diagnosing dysplasia in general, however, diagnosing the specific dysplasia may be complicated. This is particularly true prior to 24 weeks, when telltale characteristics such as femoral bowing may not be present. Prior to this gestational age, case series have shown that two-dimensional ultrasound provides an accurate diagnosis in 66% of cases. Although the precise diagnosis may not be reached prenatally, prediction of lethality appears to be excellent (96-100%), especially when cloverleaf deformity, severe rhizomelia or hypoplastic thorax were present. Three-dimensional ultrasonography or 3-dimensional Computed Tomography scanning in addition to 2-dimensional ultrasound may improve diagnostic accuracy of skeletal dysplasia's, according to some recent reports. In addition, molecular genetic testing is available; 99% of the gene mutations (in the fibroblast growth receptor 3 gene) causing either Type I or Type II Thanatophoric Dysplasia are identifiable.

Termination is an option for patients diagnosed with this abnormality. For those diagnosed too late for elective termination, or those choosing to continue the pregnancy, management decisions surround degree of neonatal support and comfort measures.

In terms of counseling about future pregnancy, recurrence risk has been reported at 0.2 – 2%, but is unlikely to be markedly increased over the general population, since these (autosomal dominant) mutations are thought to be spontaneous.