First detailed musculoskeletal study of a fetus with scoliosis and review of current literature

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SUMMARY

No papers have described, so far, the muscular anomalies present in human fetuses with scoliosis. This paper provides a detailed report along with images on the musculoskeletal structures of a fetus with scoliosis, focusing in particular on the musculature of the posterior thoracic region. The dissections reveal several anomalies in different muscle groups secondary to the severe curvature of the spine. This study, which is part of a broader attempt to describe and collect knowledge about human musculoskeletal abnormalities occurring in congenital scoliosis, as well as in a plethora of other conditions and syndromes, will likely lead not only to a greater understanding of congenital scoliosis in particular and human congenital malformations in general, but also to wider discussions on developmental and evolutionary biology. Such studies are crucial to help in the diagnosis and management options to improve quality of life in patients diagnosed with congenital scoliosis in particular.

Key words: Congenital scoliosis – Muscles – Fetuses – Birth defects – Comparative anatomy – Human anatomy

INTRODUCTION

Scoliosis is defined as an abnormal curvature of the spine, specifically at least 10 degrees in the lateral aspect, and can be characterized as congenital, idiopathic or syndromic (Altaf et al., 2013). Congenital scoliosis can be caused by either an embryological defect of vertebrae formation or a defect in vertebral segmentation (Kose and Campbell, 2004). Congenital scoliosis is yet to be linked to a known cause. Environmental factors (hypoxia, vitamin A deficiency, exposure to alcohol, valproic acid, boric acid, and hyperthermia) (Li et al., 2015), genetics, vitamin deficiencies, hormones, and drugs, have all been linked to the occurrence of vertebral defects, either individually or in combination (Hensinger, 2009). The physiologic damage develops early in the embryologic cycle, well before cartilage and bone growth, and the resultant defects can involve complete or partial fusion of the vertebrae, as well as a lack of development of the vertebrae, which can result in a curvature that can progress with time (Hensinger, 2009).

Somites are the precursors of the vertebral bodies. As the somites are formed, the development process of fetal vertebral growth in

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the human fetus starts at about 3 to 5 weeks (Erol et al., 2002; Larsen, 1997). Somitogenesis is the mechanism by which the precursor spine tissue is segmented; formation of somitogenesis happens between 20 and 30 days after conception, in the first month of pregnancy (Erol et al., 2002; Larsen, 1997). However, at 6 to 8 weeks, the somites begin to segment, and therefore congenital defects can arise long before chondrification and ossification in this process. Even earlier, during the development of the vertebral mesenchymal anlage in weeks 4 to 5, a vertebral defect can be seen for the first time (Erol et al., 2002; Larsen, 1997). The intersegmental artery and a differential in nutritional blood flow are thought to be closely linked to the development of the definitive vertebral body, as cells closest to the artery tend to divide more quickly (Tanaka and Uhthoff, 1981a, b). The problem does not seem to be caused by the notochord; however, it tends to be caused by the intersegmental arteries during resegmentation: e.g., the cartilaginous anlage of the vertebral body has been shown to have malformations, allowing for certain theories regarding the pathogenesis of congenital scoliosis (Tanaka and Uhthoff, 1981a, b). Importantly, the changes occur early in the pregnancy; no vertebral changes have been observed in fetuses older than 16 weeks (Tanaka and Uhthoff, 1981a, b). Vertebral deformities may thus be caused by a lack of vertebral development and structures, such as hemivertebra, or a failure of segmentation, causing defects of the intervertebral disk, which involves unilateral and segmented bars on the anterior and posterior sides of the spine, or a mixture of the two. Since various sections of the vertebral body and posterior elements may be involved to differing degrees, many classification schemes have been created (Tanaka and Uhthoff, 1981a, b).

So far, no papers have described the muscular anomalies present in human fetuses with scoliosis, as is also the case for many other conditions and syndromes occurring in humans. In order to reduce this key lack of knowledge, which is critical medical knowledge, in the last years Diogo and his colleagues have been actively working on the normal and 'abnormal' phenotypic embryonic and fetal development of human muscles (Alghamdi et al. 2017, 2018; Boyle et al., 2020; Crowley et al., 2019; Diogo et al., 2015a, b; 2019a, b; Gondre-Lewis et al., 2016; Karauda et al., 2021; Olewnik et al., 2018; Yurasakponget al., 2020). The present work is therefore done in the context of this wider comparative project. Namely, this paper provides the first detailed description of –including several anatomical images showing– the musculoskeletal structures of a human fetus with scoliosis, focusing in particular on the musculature of the posterior thoracic region. Due to the rarity of human fetuses with scoliosis that are available for dissection, information about a single individual is indeed a crucial contribution to comparative and pathological human anatomy. Specifically, this paper compares the results obtained with the very scarce anatomical information available in the literature about this condition, and discusses the data gathered, taking into account previous observations by the authors concerning other medical conditions and broader current evolutionary and developmental discussions.

MATERIALS AND METHODS

A male fetus with scoliosis –approximately between 16 to 20 gestational weeks– was dissected at Rui Diogo's lab, Department of Anatomy, Howard University College of Medicine (Fig. 1). The fetus is part of a collection obtained in the 1980s by Professor Aziz, which was donated to Diogo's lab for research. It was preserved in alcohol. Standard microdissection instruments were used for the dissections. The microdissections were bilateral and mostly focused on muscles, with nerves and major blood vessels maintained wherever possible. The deeper muscles were observed after the superficial muscles were cut close to their attachment. Complete detachment was avoided in order to maintain the muscle's integrity for future research. The following characteristics of each muscle were observed: 1) presence/absence, 2) origin, 3) insertion, 4) variation in number of bellies and/or tendons, and 5) overall muscular configuration. Muscles were compared to those of 'normal' human adults as well as 'normal' fetuses, based on descriptions based on works by Diogo and colleagues (see above). At each point of the

dissection, images were taken as a guide using a professional Nikon D90 camera with an AF-S Micro NIKON 60 mm lens to record various anatomical regions. To highlight a particular muscle, close images were taken and labeled accordingly. For size comparison, each photograph included a regular centimeter scale.

RESULTS

External features

Upon inspection of the posterior thorax, severe curvature of the spine is appreciated with overall appearance of the fetus leaning to the left side (Figs. 1-2). There is also evidence of tilted, uneven shoulders, with the left shoulder blade protruding more than the right, prominence of the ribs on the left side, and uneven waistline with the left hip higher than the contralateral side.

Posterior thoracic Musculature

Upon reflecting the left trapezius, measurements revealed that the left trapezius was approximately 0.5 cm greater than the right side. Apart from this, the trapezius of both sides has a normal configuration, attaching to the spinous processes of the vertebrae C7-T12, the spine of the scapula, and the superior nuchal line (Fig. 3). A thin muscle layer of the latissimus dorsi was appreciated bilaterally, of approximately equal measurements, and a normal configuration, attaching to the vertebral spines from T7 to the sacrum and inferior angle of the scapula (Fig. 4). The levator scapulae also has a normal overall configuration, originating from the transverse processes of C1-C4 vertebrae, but was abnormally fused with the trapezius muscle (Fig. 5). The splenius capitis has a normal configuration, attaching to the ligamentum nuchae and spines of C7-T6 vertebrae (Fig. 6). The

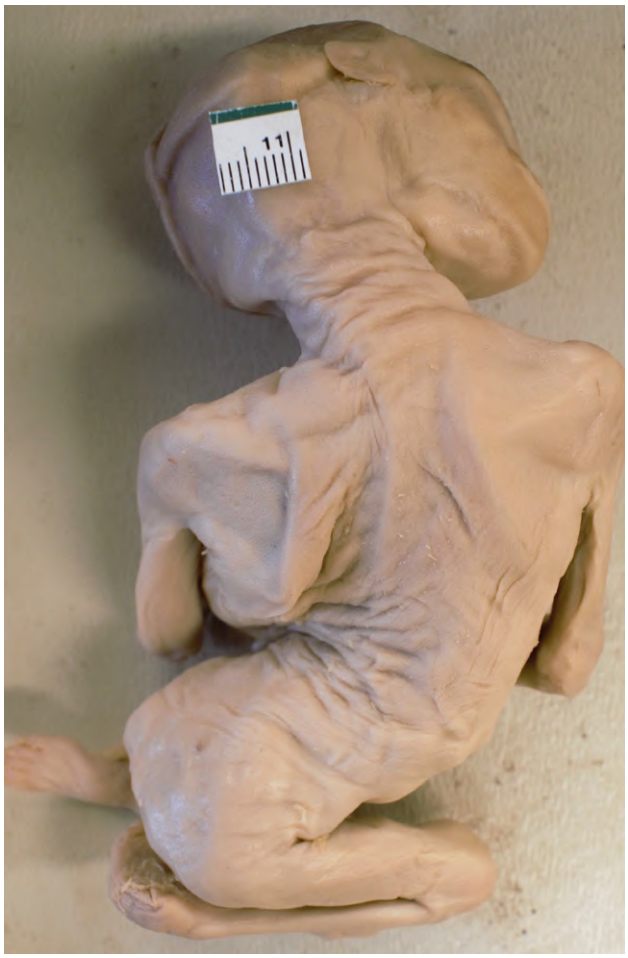

Fig. 1.- Posterior view of the fetus, showing a prominent left sided curvature of the spine.

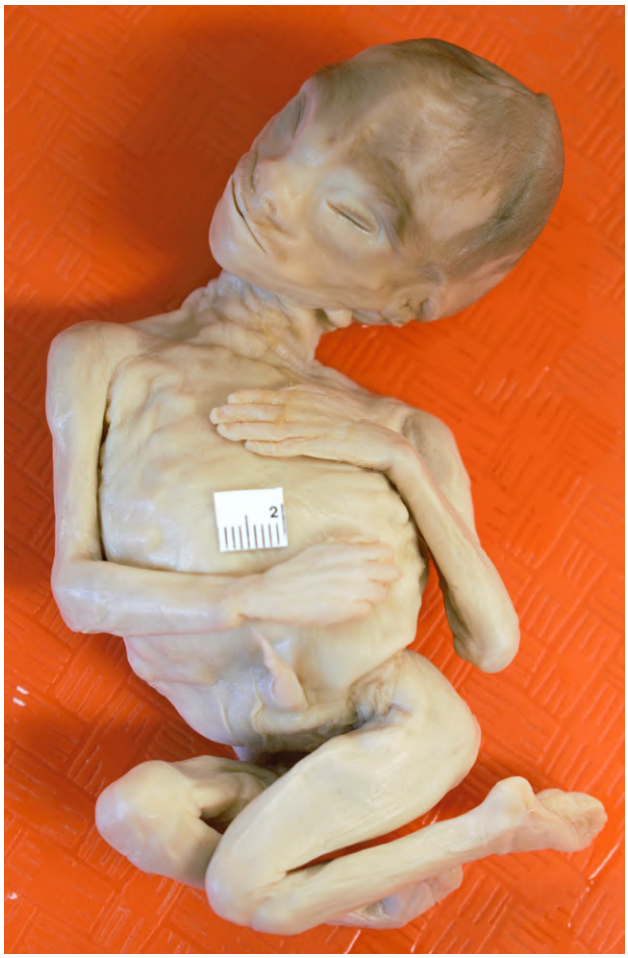

Fig. 2.- Anterior view of the fetus, showing a prominent left sided curvature of the spine.

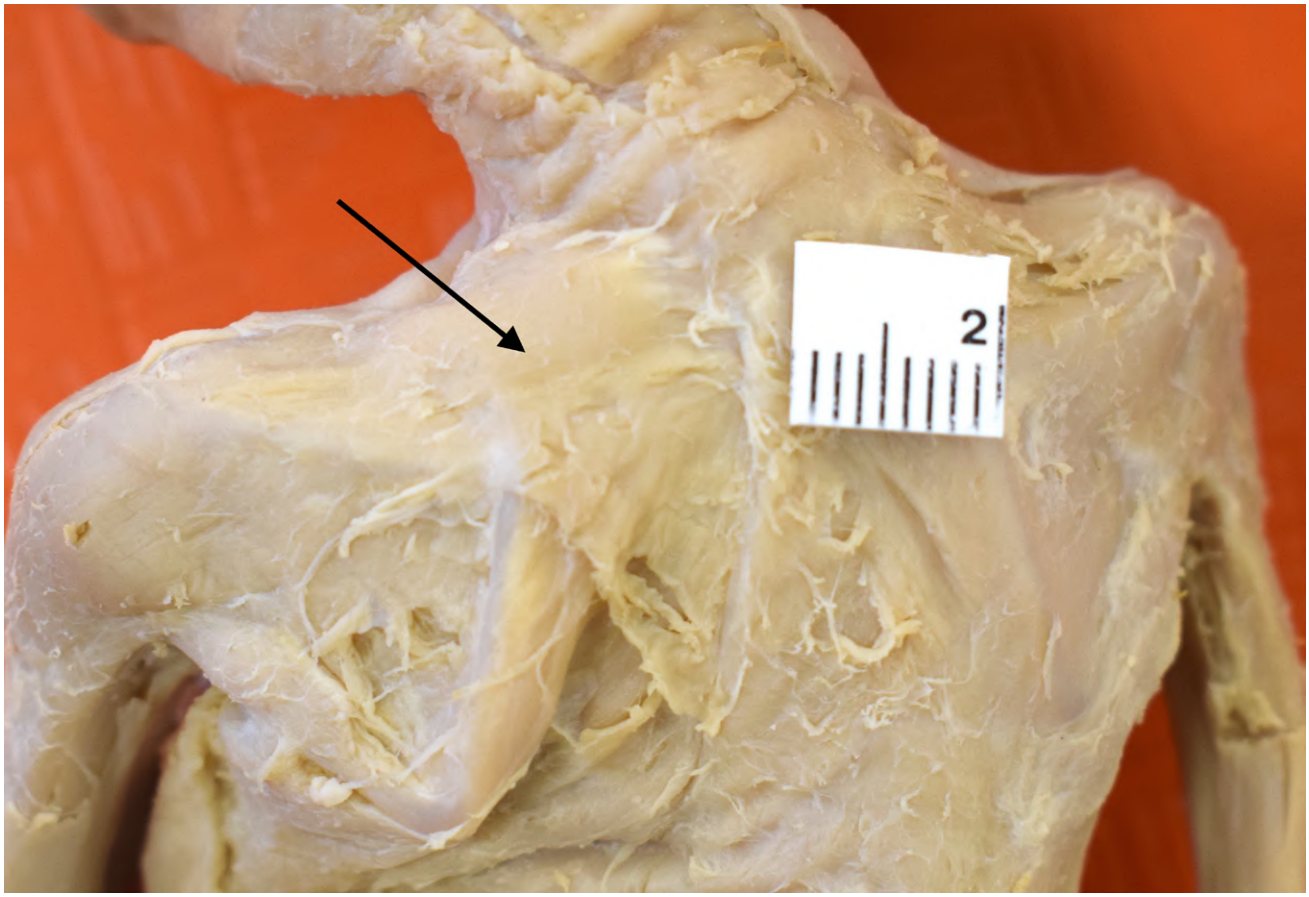

Fig. 3.- This image shows the trapezius muscle properly attached to the spinous processes C7-C12, spine of the scapula and the superior nuchal line.

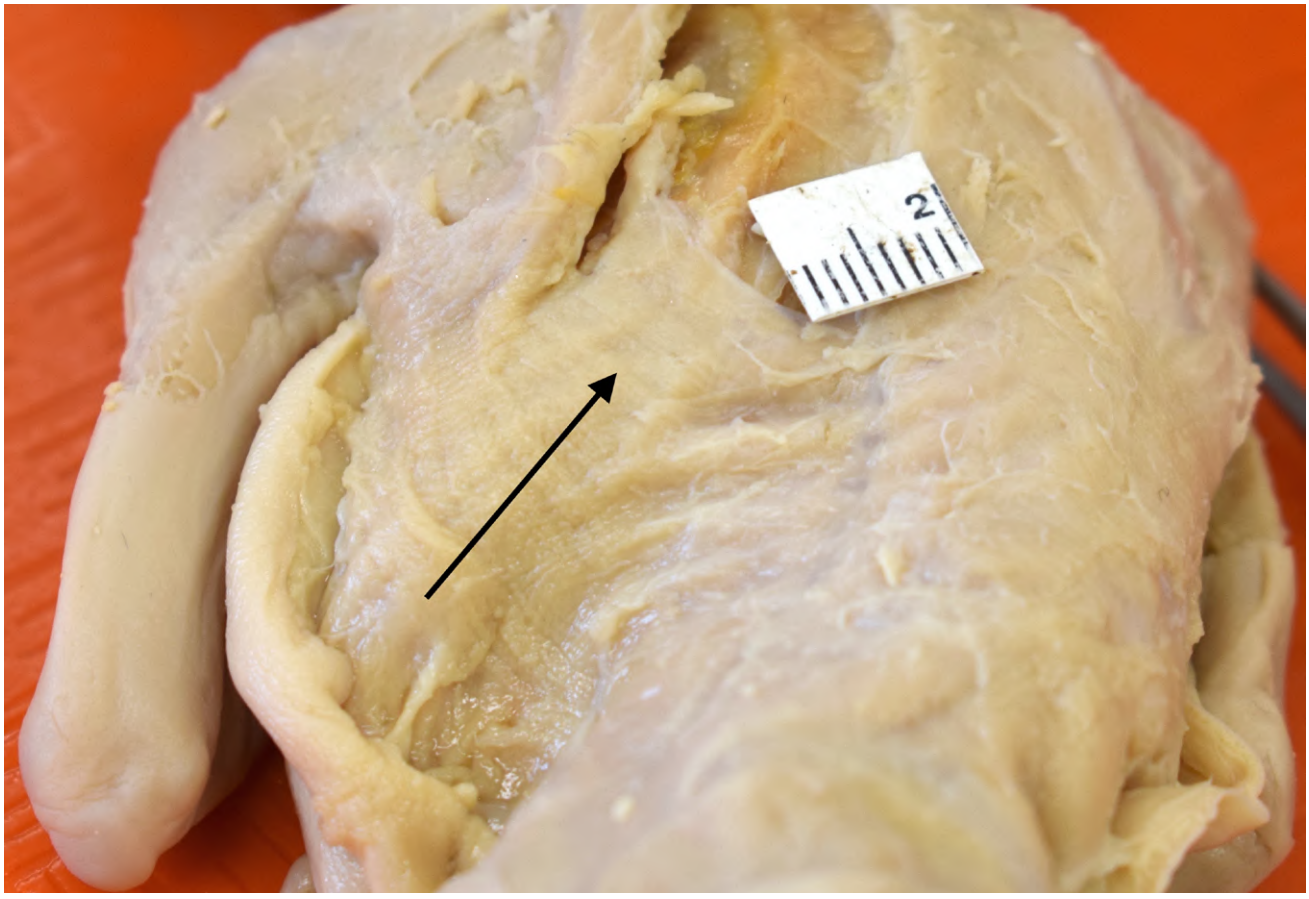

Fig. 4.- View showing of the latissimus dorsi.

supraspinatus, infraspinatus, and teres minor had mainly normal attachments (Fig. 7): distally to the superior, middle, inferior facets on the greater tubercle of the humerus, respectively. There was a thin layer of short muscle fibers between the medial border of the scapula and the neural tissues in the back, which seemed to correspond to a very underdeveloped rhomboid major and minor. Erector spinae muscles were fused and difficult to distinguish (Fig. 8). The other muscles of the body seemed to have the typical configuration for a male fetus of this age. In Table 1 we summarize the muscular anomalies we found in this fetus.

Table 1. Normal musculature vs. anomalous musculature observed in a fetus with congenital scoliosis.

Normal musculature	Anomalous musculature
Trapezius muscle approximately equal lengths bilaterally	Trapezius muscle 0.5 cm greater on left than right
Levator scapulae separated from trapezius	Levator scapulae fused with trapezius
Erector spinae muscles separate into spinalis, Longissimus, and iliocostalis	Erector spinae muscle fused

DISCUSSION

Since small spinal deformities frequently go undetected, the true incidence of congenital scoliosis in the general community remains unknown. Congenital intervertebral or vertebral body defects cause an imbalance in the trunk's longitudinal development in around 10% of cases of structural scoliosis (Burnei et al., 2015; Hedequist and Emans, 2004, 2007; Oestreich et al., 1998). Girls have a 2.5:1 chance of developing congenital scoliosis compared to boys (Jaskwhich et al., 2000; Konieczny et al., 2013). Curves appear equally often to the left and right. The incidence of the curve varies by degree of the spine: upper thoracic: 33%, lower thoracic: 31%, thoracolumbar: 20%, lumbar: 11%, and lumbosacral: 5% (Terminology Committee, 1976). The affected fetus in our case was a male, which is not consistent with the recorded higher frequency of females relative to males.

In the male fetus analyzed for this study, it was observed that various anomalies occur in the musculoskeletal system (Figs. 1-8; Table 1). Other studies have shown that patients with

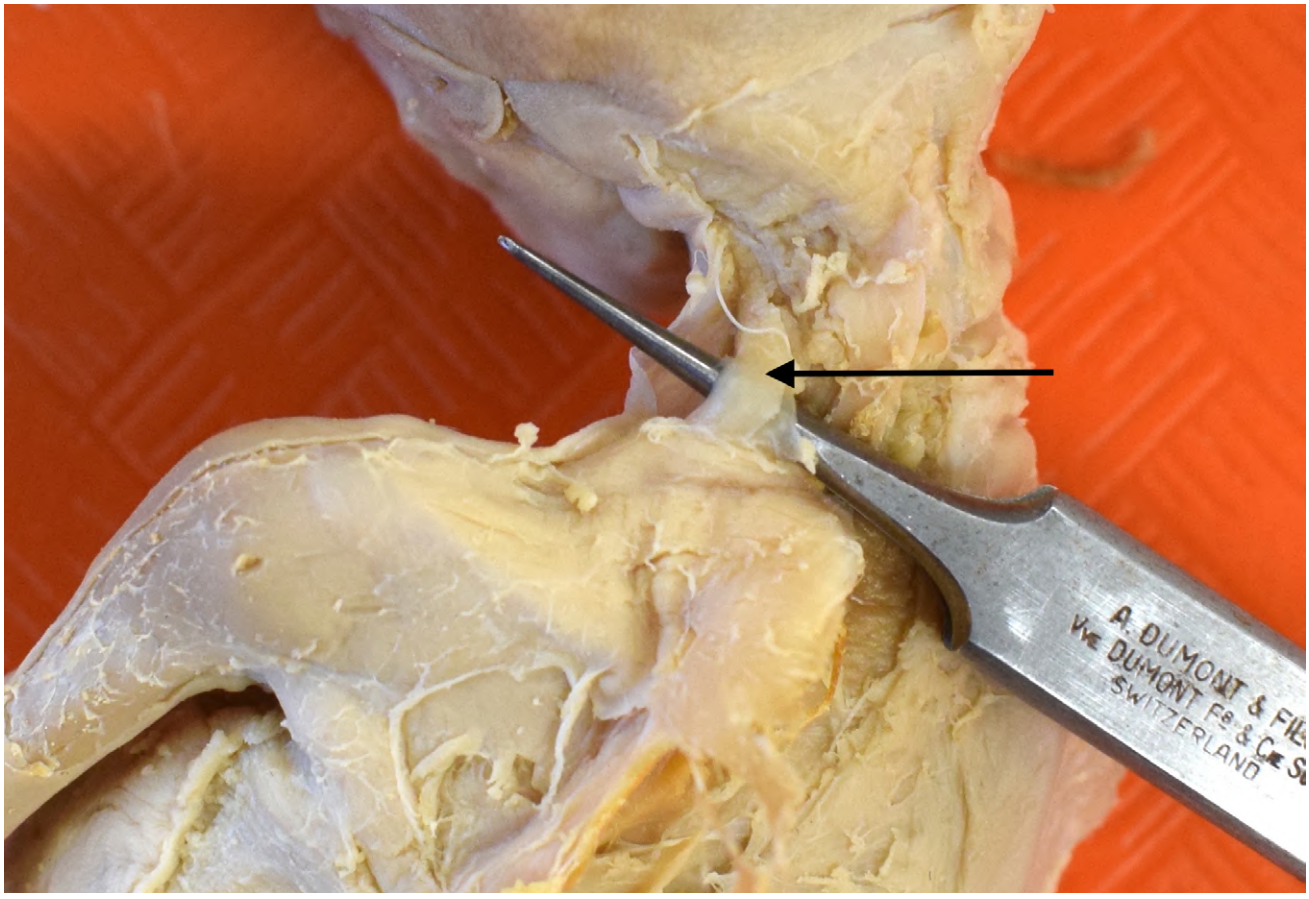

Fig. 5.- View showing the left levator scapulae abnormally fused to the trapezius muscle.

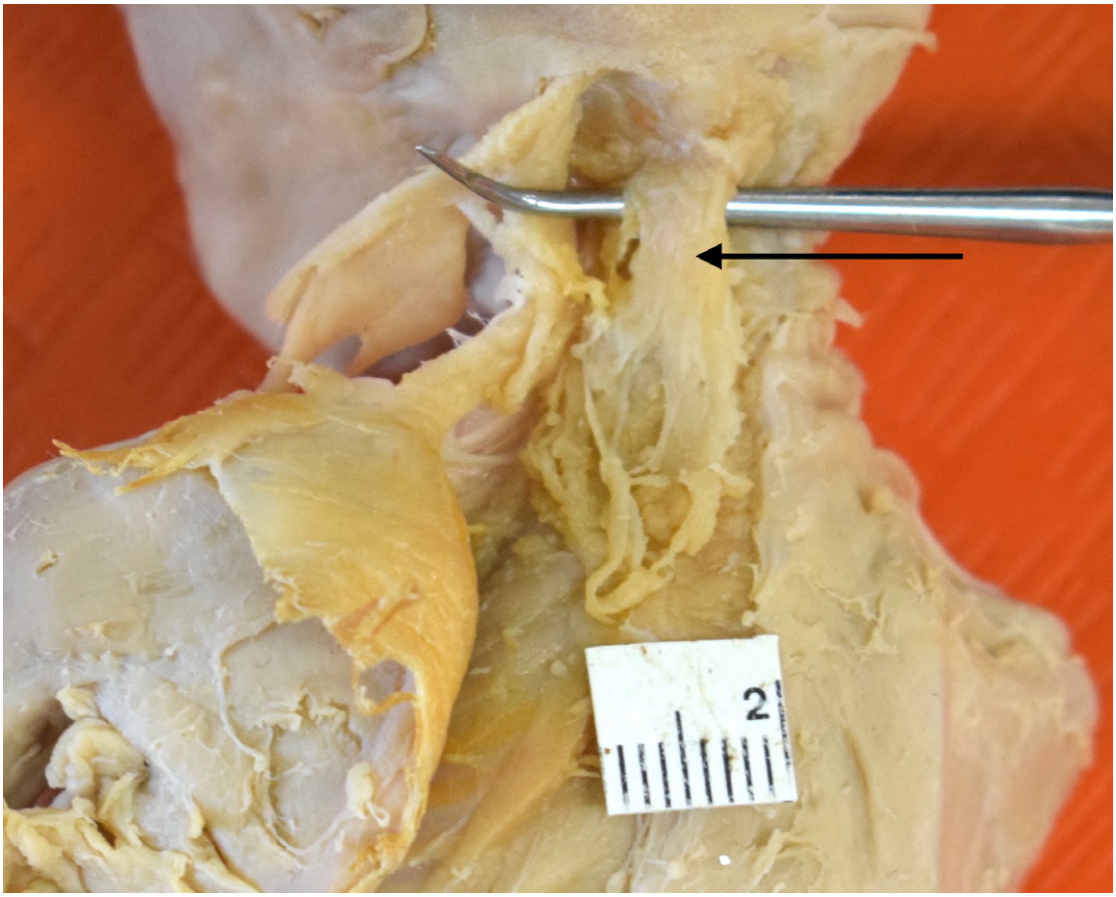

Fig. 6.- View showing the splenius capitis attached to the ligamentum nuchae and spines of C7-T6 vertebrae.

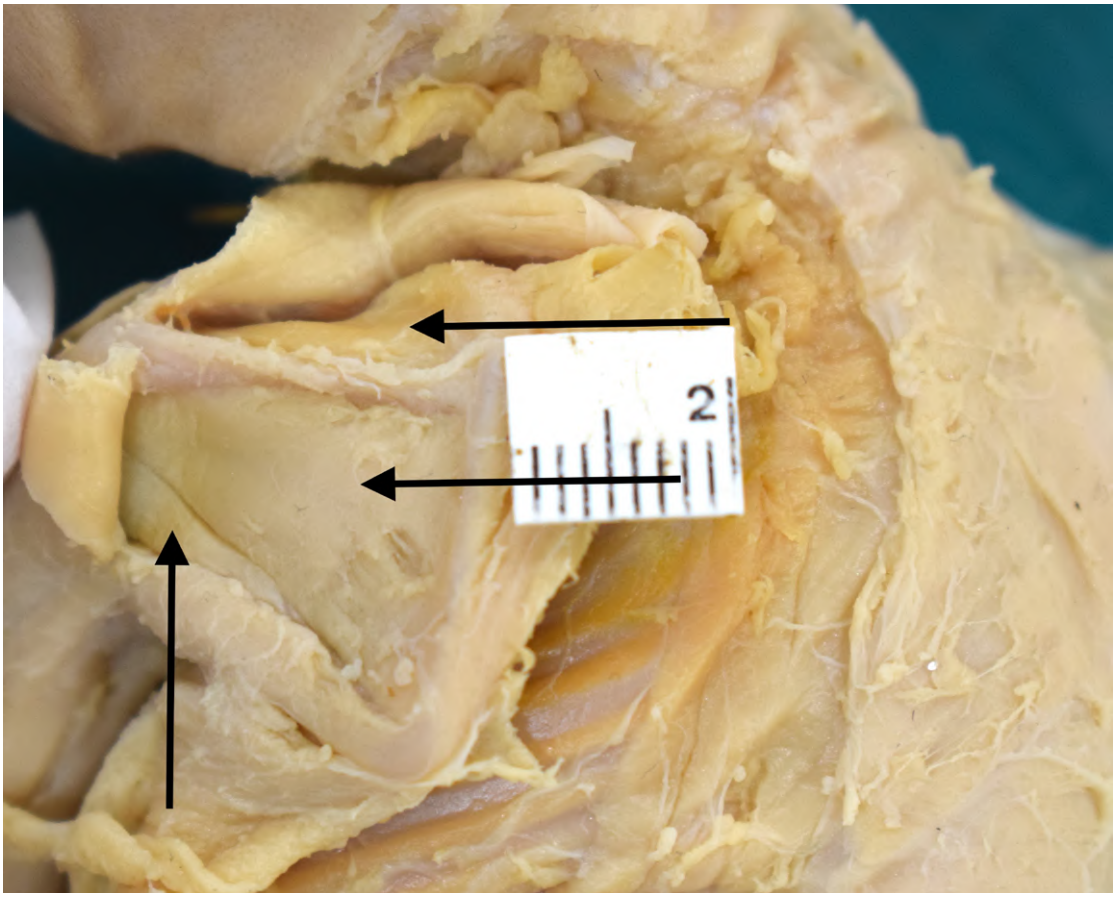

Fig. 7.- View showing the supraspinatus, infraspinatus and teres minor attached distally to the superior, middle, inferior facets on the greater tubercle of the humerus, respectively.

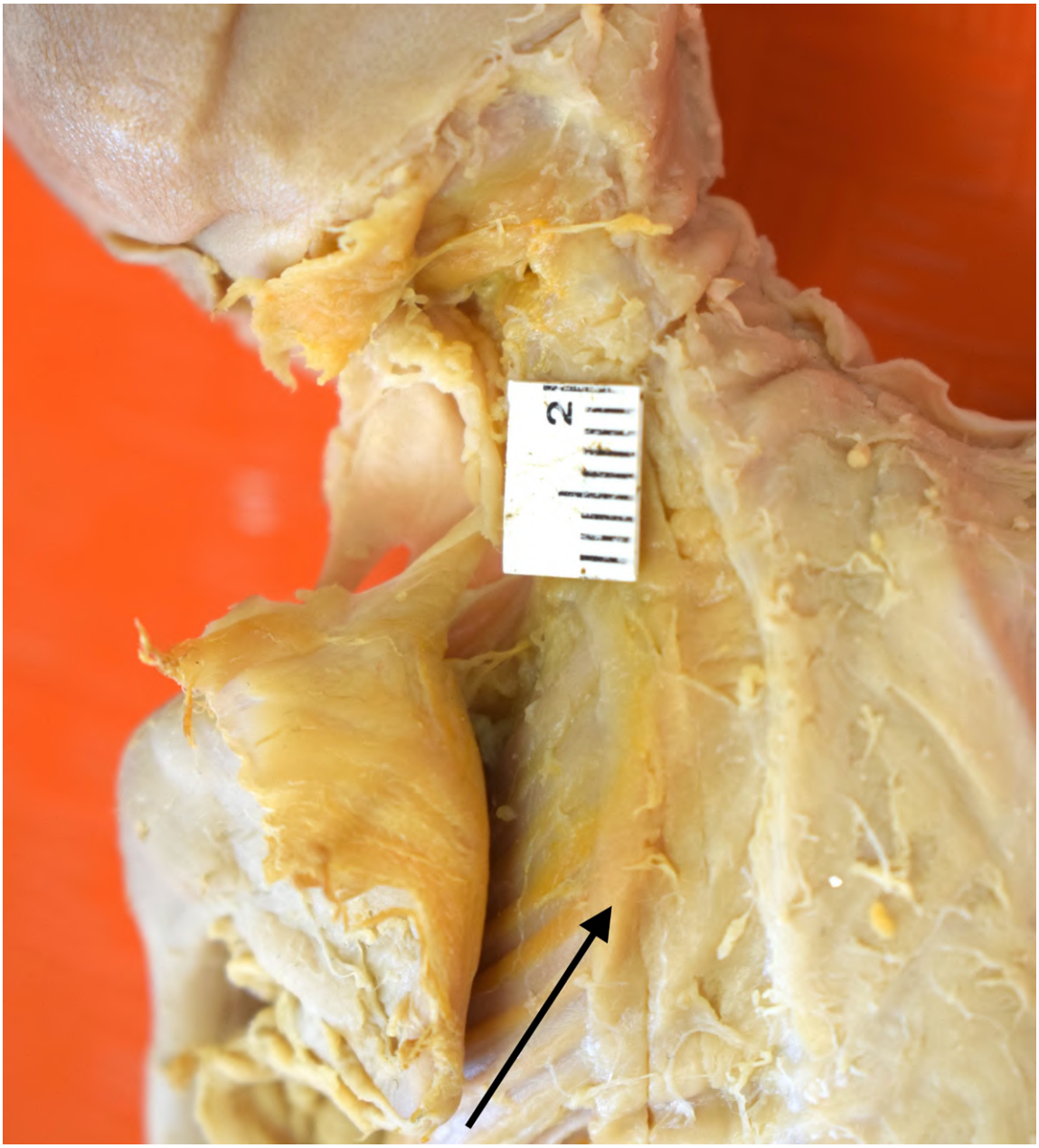

Fig. 8.- View showing of the erector spinae muscles which were fused together.

congenital scoliosis may have anomalies in other organ systems in as many as 61 percent of cases (Beals et al., 1993; Shen et al., 2013). Since the spine, genitourinary tract, musculoskeletal system, and cardiovascular system all develop during similar times, an embryonic insult to one or more of these systems may occur. Therefore, defects of one system should prompt evaluation of the other related systems to be evaluated as well. For instance, congenital spinal deformity is also linked to clubfoot, developmental dysplasia of the shoulder, limb hypoplasia, and Sprengel's deformity (Hensinger, 2009). Overall, the patient must be evaluated extensively for musculoskeletal abnormalities, as these are the most prominent organ system anomalies involved with congenital scoliosis (Hedequist and Emans, 2004, 2007). Since congenital abnormalities are linked to congenital scoliosis in the thoracic and lumbar spine, the entire spine, including the cervical spine, must be examined (Arlet et al., 2003; Beals et al., 1993).

However, as noted above, not only such correlational studies are missing in the literature, but even detailed studies of soft tissue anomalies seen in specific conditions, such as scoliosis, are also missing in the literature, which prevents a deep knowledge and understanding of birth

defects in general. In this study, the first detailed one of a fetus with scoliosis, did reveal a series of muscle anomalies, including abnormal muscle lengths and fused muscles (Table 1). However, further studies are needed to determine if these anomalies are consistently present in other fetuses having this condition, as well as in other organ systems. It is absolutely crucial to study correlational features and associated syndromes in detail, because the detection of less apparent defects can have a significant impact on the patient's overall well-being, maybe even more so than the discovery of more obvious defects. Additionally, the best management of these complex spine deformities would require a complete knowledge of the natural history of the deformity, as well as treatment principles. New imaging techniques such as three-dimensional computed tomography (CT) and magnetic resonance imaging (MRI) are useful for studying the underlying deformity and learning how dynamic deformities evolve (Van Goethem et al., 2007). Careful monitoring with radiographic assistance aids in determining if surgical intervention is needed (Van Goethem et al., 2007).

However, it should be pointed out that, at this point, current techniques, including MRI, often do not allow to mirror the fine details that can be detected in microdissections, such as the very tiny abnormal bundles of fibers connecting muscles such as trapezius and the levator scapulae in the fetus dissected by us. Therefore, studies such as this one are crucially needed for a greater understanding of congenital scoliosis in particular, but also of human congenital malformations in general, as well as to help in the diagnosis and management options to improve quality of life in patients diagnosed with congenital scoliosis in particular.

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