Congenital Anatomical Variant of the Clavicle

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ABSTRACT
The aim of this study is to present a rare abnormality of the clavicle (Code: SGS01) that was discovered in an ossuary in the Church of San Gaetano (Sulmona, central Italy; XVII–XIX centuries CE). In the middle third, the clavicle had three areas with losses of substance in the form of oval-shaped foramina with maximum diameters of 1–2 cm that were located in the anterior and superior surfaces of the diaphysis. The margins of these foramina were well defined and rounded, and the surfaces of the canal walls were smooth. Additionally, there were no zones of bony activity or reactive changes around the foramina. This new congenital anomaly of the clavicle and blood vessels is consistent with a variant that might have originated during fetal growth in which the subclavian vein or artery remained included during the process of ossification of the clavicle. Anat Rec, 300:1401–1408, 2017. © 2017 Wiley Periodicals, Inc.

Key words: paleopathology; anthropology; bone anomaly; circulatory disturbances; blood vessels

The clavicle is a bone with a complex structure that has an important role in the stability and movement of the shoulder girdle. In recent years, morphological studies of the clavicle have aroused great interest among researchers. For physical anthropologists, the clavicle is a source of information about the adaptive and evolutionary processes from the perspective of comparative anatomy and functional morphology (Shankhyan, 1997; Voisin, 2006, 2008). The various enthesopathic lesions of the clavicles and their distribution patterns in ancient human populations are related to the health statuses and lifestyles of those populations (Capasso and Di Domenicantonio, 1998).

For forensic anthropologists, the clavicle is a useful bone that allows for the reconstruction of the biological profile of an individual in judicial contexts related to, for example, sex, age at death, and handedness (McCormick et al., 1991; Black and Scheuer, 1996; Mays et al., 1999; Auerbach and Raxter, 2008; Danforth and Thompson, 2008; Akhlaghi et al., 2012; Papaioannou et al., 2012; Milenkovic et al., 2013). For orthopedic surgeons and traumatologists, the clavicle is important in terms of improving the treatments of fractures and pathological complications (Andermahr et al., 2007; King et al., 2014; Rockwood and Matsen III, 2009; Sinha et al., 2011; Walters et al., 2010). Thus, the anatomy of the clavicle and any anomalies in its morphology are of great interest across various disciplines.

MATERIAL AND METHODS

The object of our study is a left clavicle (Fig. 1; code: SGS01) that was found in an ossuary that included a total of 1,088 individual skeletons. These skeletons were exhumed from under the floor of the Church of San Gaetano in the city of Sulmona (L'Aquila, Italy), which has

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Fig. 1. Different views of the left clavicle (SGS01) from Sulmona illustrating the three areas with losses of substance that form oval-shaped foramina; one foramen is located on the superior surface, and the other two are on the anterior surface.

TABLE 1. Anthropometric measurements of clavicle SGS01

Measurement	Definition	Value (mm)
Maximum length[a]	Maximum distance from the sternal to the scapular end of the clavicle	139.10
Midshaft vertical diameter[a]	Distance from the superior to the inferior surface at midshaft	17.34
Midshaft sagittal diameter[a]	Distance from the anterior to the posterior surface at midshaft	16.15
Midshaft circumference[a]	Circumference taken at the midpoint of the diaphysis	55.10
Maximum breadth of sternal end[b]	Maximum breadth of the sternal end taken perpendicularly to the shaft	21.77
Acromial breadth	Maximum width of the acromial end of the clavicle	12.51
Acromial height	Maximum height of the acromial end of the clavicle	8.78

[a]From Martin and Knußmann (1988).
[b]From Papaioannou et al. (2012).

been dated to between the XVII and XIX centuries CE. Clavicle SGS01 could not be assigned to any particular skeleton. Clavicle SGS01 is now stored in the University Museum of the 'G. d'Annunzio' University of Chieti–Pescara (Italy).

Seven measurements of clavicle SGS01 were acquired with digital calipers, an osteometric board, and flexible tape (Table 1).

RESULTS

Based on its dimensions, this specimen falls inside the range of normal variability of the human clavicle, and it has been attributed to an adult female individual. The sex was defined by applying the formulae developed by Murphy (1994), Alemán et al. (1997), Frutos (2002), Tise et al. (2013), and Králík et al. (2014) in which the maximum length of the clavicle is used as the only relevant variable. Indeed, due to the morphological anomalies of the bone, which were particularly evident in the midshaft, no other dimensions of clavicle SGS01 proved useful for sex estimation. Moreover, the defined sex should be interpreted with caution due to the different population origins of the formulae used for the sex assessment.

In the medial third of the diaphysis, clavicle SGS01 exhibits three areas with loss of substance in the form of oval-shaped foramina; one foramen is on the superior surface, and other two are on the anterior surface (Fig. 1). The superior foramen has a maximum diameter of 11.12 mm and a minimum diameter of 6.15 mm. For the anterior surface, the medial foramen has a maximum diameter of 20.35 mm and a minimum diameter of 9.51 mm, and the lateral foramen has a maximum diameter of 17.85 mm and a minimum diameter of 9.16 mm. These three foramina are connected by a canal with a maximum diameter of 10.54 mm.

The margins of these foramina are well-defined and rounded, and the surfaces of the canal walls are smooth. The cortical bone of the canal is well preserved and not connected to the medullary canal. No zones of bony activity or reactive changes were observed around these

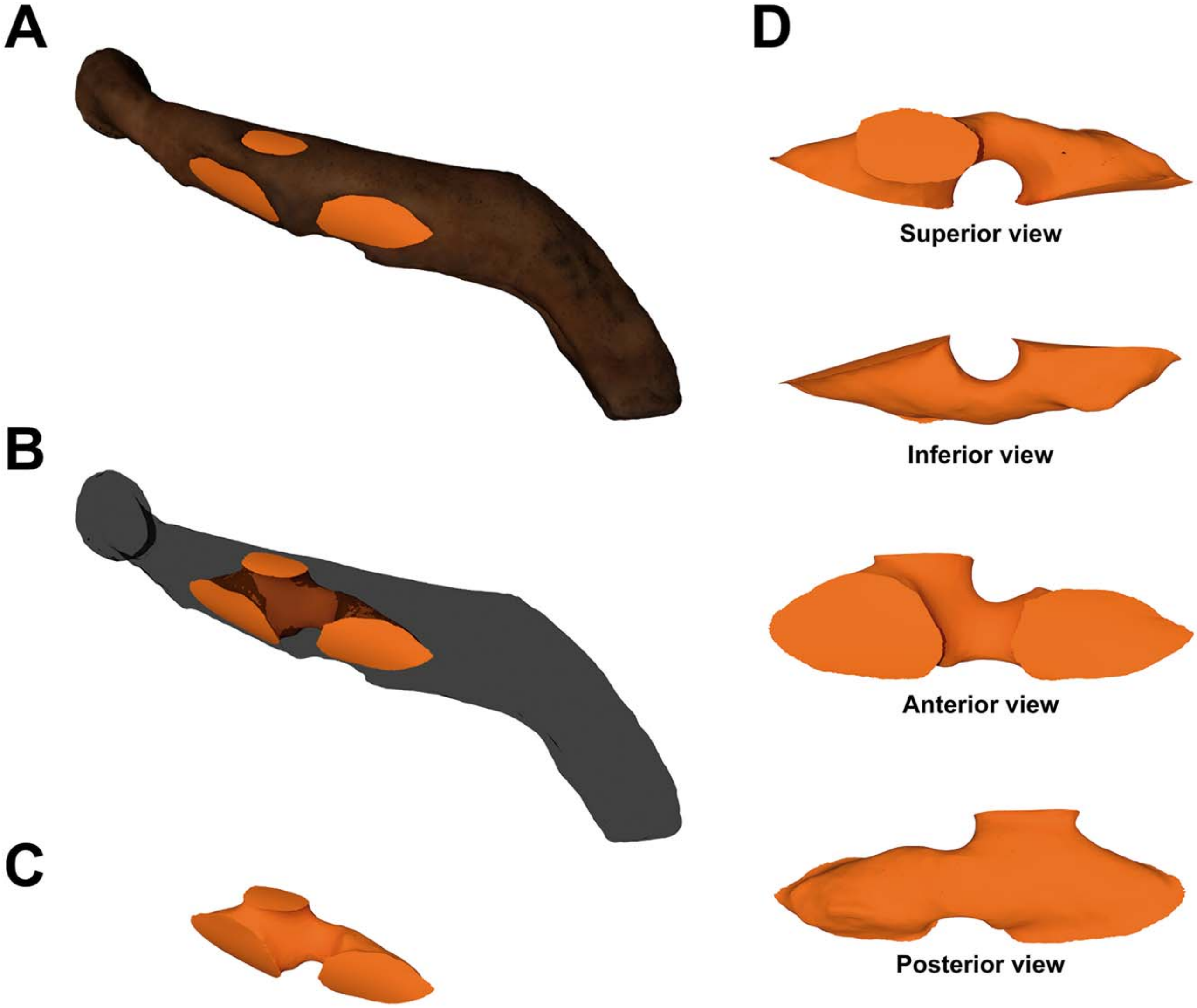

Fig. 2. Depiction of the shape of the negative space created within the shaft of clavicle SGS01 by the three foramina. **A**: Original illustration of clavicle SGS01 showing the negative space in orange. **B**: Semi-transparent depiction of the clavicle illustrating the morphology and distribution of the negative space. **C**: Morphology of the negative space isolated from the clavicle. **D**: Different views of the negative space created within the shaft of the clavicle.

foramina. The shape of the negative space created within the shaft of the clavicle by these foramina is consistent with that expected with the passage of a vessel (Fig. 2).

The entheseal changes at the muscular insertions are not marked except at the areas of attachment of the pectoralis major and deltoid muscles. Clavicle SGS01 exhibits a marked imprint of the pectoralis major muscle with a slight modification of the surface that appears slightly flattened and the presence of osteophytic formations of up to 1 mm (grade 1 according to Mariotti et al., 2004 and grade 2 according to Donatelli and Scarsini, 2006). A slight osteophytic formation is also observable on the bone bridge separating the medial and lateral foramina at the anterior surface. The imprint of the deltoid muscle exhibits an irregular surface and the presence of clear osteophytic formations that protrude slightly from the cortical surface (grade 2 according to Mariotti et al., 2004 and grade 3 according to Donatelli and Scarsini, 2006).

Microscopic analysis demonstrated the absence of any periosteal reactions, bony formations, or indications of healing. The X-ray analysis did not indicate any signs of trauma and revealed that the margins of the foramina and the walls of the connecting canal are not bordered by sclerotic bone, the presence of which is usually related to infections or other diseases (Fig. 3). Moreover, computed axial tomography revealed normal internal bone structure. Overall, clavicle SGS01 does not present pathological signs that could be related to traumatic events or infectious or metabolic diseases that occurred during the life of the individual.

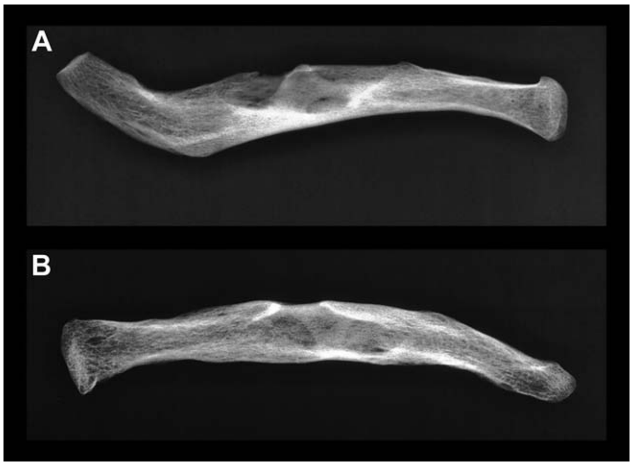

Fig. 3. Supero-inferior (**A**) and antero-posterior (**B**) radiographic images of clavicle SGS01 revealing the lack of zones of bony activity and reactive changes around the foramina.

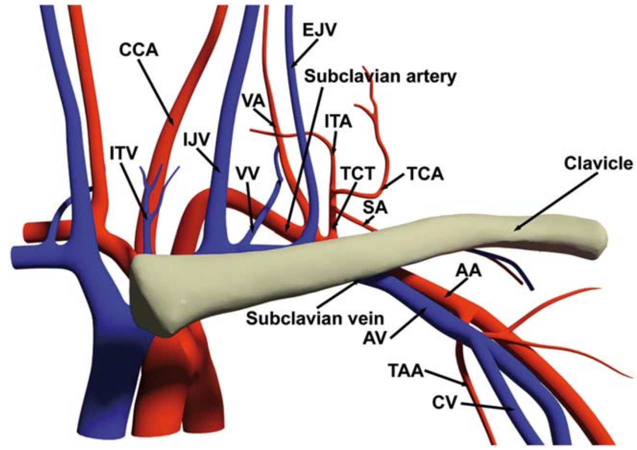

Fig. 4. Anatomical relationship between the left clavicle and the adjacent major blood vessels. AV, axillary vein; AA, axillary artery; CCA, common carotid artery. CV, cephalic vein; IJV, internal jugular vein; EJV, external jugular vein; ITV, inferior thyroid vein; ITA, inferior thyroid artery; SA, suprascapular artery; TAA, thoracoacromial artery; TCT, thyrocervical trunk; TCA, transverse cervical artery; VV, vertebral vein; VA, vertebral artery.

DISCUSSION

Relevant Features in the Development of the Clavicle and the Anatomy of the Neurovascular Bundle

The clavicle. The clavicle is the first bone to become ossified during embryogenesis through a process known as intramembranous ossification. This process begins in the 5th and 6th weeks of gestation from two nearby primary ossification centers, one of which is medial and the other is lateral (Fawcett, 1913; Ogden et al., 1979; Ogata and Uhthoff, 1990; Scheuer and Black, 2004). Shortly after ossification commences during the 7th week of intrauterine life, a bony bridge forms between the two centers of ossification with vascular invasion of the ossified matrix (Fawcett, 1913). Cartilaginous growth areas known as enchondral ossifications develop at both the acromial and sternal ends of the bone, although the ossification at the sternal end appears to be the dominant longitudinal growth region.

Finally, from 15 to 18 years of age, a secondary ossification center shaped like a disc appears in the sternal end of the clavicle. This ossification center begins to fuse with the clavicular diaphysis between 18 and 25 years of age, and it is completely fused by 25 to 31 years of age (Scheuer and Black, 2004; Rockwood and Matsen III, 2009).

Therefore, an unusual situation of the coexistence of membranous diaphyseal and metaphyseal ossification with enchondral longitudinal growth in the same bone exists in the clavicle. Intramembranous ossification of the diaphysis primarily contributes to longitudinal growth during both the intrauterine and postnatal periods. In contrast, there is no significant longitudinal growth at the acromial end of the clavicle (Freyschmidt, 2003). Thus, the clavicle is the first bone to ossify during embryogenesis; however, after birth, it is the last bone to reach full maturity.

The neurovascular bundle. The neurovascular bundle is composed of the subclavian vessels and the brachial plexus, and at the superior aperture of the thorax, it passes through three anatomical compartments to reach the upper extremities on each side of the body. From medial to lateral, the brachial plexus and subclavian artery pass through the following structures: (i) the scalene triangle, which is bounded by the anterior and middle scalene muscles; (ii) the costoclavicular interval, which is bounded by the clavicle and the first rib; and (iii) the retropectoralis space, which is bounded by the posterior margin of the pectoralis minor muscle and the anterior chest wall. The subclavian vein exhibits a slightly different course; it first passes anterior to the anterior scalene muscle and subsequently joins the brachial plexus and subclavian artery to pass through the costoclavicular interval and retropectoralis space (Testut, 1943; Urschel and Kourlis, 2007; Rockwood and Matsen III, 2009). Thus, the costoclavicular interval is the anatomical region in which the brachial plexus and both of the subclavian vessels pass in close proximity to the clavicle and the first rib.

In addition to the differences in the courses of the subclavian vessels by the shoulder girdle, they also differ in size. In healthy adult individuals, the range of variation of the diameter of the left subclavian artery diameter is from 8 to 11 mm (Testut, 1943; Kahraman et al., 2006; Coselli and Lemaire, 2008; Alsaif and Ramadan, 2010), and the diameter of the left subclavian vein ranges from 7 to 12 mm (Testut, 1943; Mitchell and Clark, 1979; Fortune and Feustel, 2003; Boon et al., 2007; Hurst, 2014), with the diameter of the vein generally the larger of the two within an individual. The diameters of the subclavian artery and vein correspond to those of the canal and foramina and these vessels would pass nicely through them.

Relationship between the clavicle and its adjacent vascular structures. Regarding the anatomical relationship, in terms of distance and direction, between the clavicle and the adjacent major blood vessels, Sinha et al. (2011) described that the subclavian vessels lay posteriorly and inferiorly in the middle third of the clavicle (Fig. 4). The mean angles of lines joining

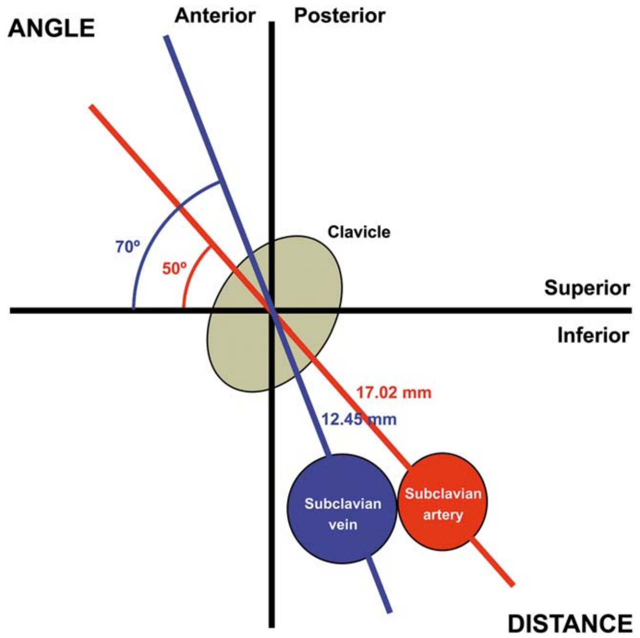

Fig. 5. Illustration showing the subclavian artery and vein in relation to the clavicle at the middle third in terms of distance and direction.

the center of the clavicle and with the centers of the subclavian artery and vein relative to horizontal are 50° (range: 12°–80°) and 70° (range: 38°–100°), respectively. Here, the mean distances of the subclavian artery and vein from the clavicle are 17.02 mm (range: 5.40–26.80 mm) and 12.45 mm (range: 5.00–26.10 mm), respectively (Fig. 5).

Clavicle SGS01

The clavicle is curved and is thinner in the middle third to accommodate the vascular bundle, which passes between it and the first rib at this point. As we have demonstrated, the location of the anomaly observed in clavicle SGS01 corresponds with this costoclavicular interval in which there is a close relationship between the clavicle and the subclavian vessels during development.

Entheseal changes. The muscular insertions are not large except at the area of the attachment of the pectoralis major and deltoid muscles. Several muscles of the neck and shoulder attach to the clavicle; however, the pectoralis major and deltoid are the muscles that attach proximally along a line that passes longitudinally between the anterior and superior foramina. The pectoralis major originates from the anterior portion of the medial two-thirds of the clavicle, and the deltoid muscle originates on the anterior portion of the inner surface of the lateral curve of the clavicle (Rockwood and Matsen III, 2009). In clavicle SGS01, the imprints of these two muscles extend to topographical areas that correspond to the normal anatomical locations. The pectoral major and deltoid muscles are currently considered to be an agonist pair in the muscular set that controls shoulder joint movement and is responsible for the forward flexion and medial rotation of the arm (Aiello and Dean, 2002). The enlarged muscle attachment sites on clavicle SGS01 suggest that this individual engaged in an activity that placed stress on the left shoulder with emphasis on the forward flexion and medial rotation of the arm (Chapman, 1997; Capasso et al. 1999). However, without the soft tissues and the other bones of the pectoral girdle the possible functional implications of these foramina and the passage of the blood vessel through the clavicle are quite difficult to discuss.

Abnormalities and pathological conditions. The clavicle is subject to pronounced morphological abnormalities and pathological conditions (e.g., Kim et al., 2007; Curraino and Herring, 2009; Frangos et al., 2011; Figueiredo et al., 2012; van der Meijden et al., 2012; Shukla et al., 2014), and generally, there should be little difficulty in distinguishing these diseases and anomalies from normal variants of the clavicle (Freyschmidt, 2003).

In terms of such morphological variations, small defects have been observed occasionally in the superior border of the middle third of the clavicle, which represent the foramen of a canal through which the medial fascicle of the supraclavicular nerve passes. The position and location of this canal are thus related to the course of the intermediate supraclavicular group of nerves but, at the same time, the diameters of the foramina are larger than it would be expected from these small nerves. According to anatomists, this nerve canal is present in 2% to 6% of the population (Freyschmidt, 2003; Jelev and Surchev, 2004, 2007; Natsis et al., 2007, 2015). Neural foramina and nutrient canals also occur in the clavicle, and these are more conspicuous at the junction of its middle and lateral thirds (Freyschmidt, 2003; Jelev and Surchev, 2004, 2007). Waern (1933/1934) (cited in Jelev and Surchev, 2007) reported a case of a blood vessel (i.e., a small vein) that traversed the clavicle, together with a supraclavicular nerve branch. This same author indicated that it is also possible for the clavicle to be penetrated by a vein or an artery; however, this condition has not been confirmed in the scientific literature to date.

Pathological events can affect the clavicle and alter its morphology. Indeed, chronic recurrent multifocal osteomyelitis is an inflammatory disease that exhibits a predilection for the clavicle. This disease is an autoinflammatory disorder that occurs in children and young adults and is characterized by nonbacterial osteomyelitis. In such cases, the clavicle is enlarged and exhibits increased density. Moreover, in the advanced stage, the clavicle exhibits lytic and sclerotic lesions (Freyschmidt, 2003; Khanna et al., 2009).

Congenital syphilis is a bacterial disease that can be transmitted *in utero* from a mother during the early stage of the disease. Congenital syphilis is a well-known cause of various skeletal problems, and the clavicle exhibits a predilection for osseous involvement. In the advanced stages, bony pathologies can resemble those of periostitis, osteitis, osteochondritis and osteomyelitis. Syphilitic osteomyelitis typically develops in the metaphyseal region. Moreover, periosteal reactions can result in destructive lesions in the medial third of the clavicle in combination with the extensive formation of new bone (Rasool and Govender, 1991; Freyschmidt, 2003; Kim et al., 2007). Other signs of congenital syphilis include what is known as Higoumenakis' sign, which refers to the enlargement of the sternal end of the clavicle (Frangos et al., 2011).

Congenital pseudarthrosis of the clavicle is a rare entity of unknown etiology. The pathogenesis of this entity is related to the embryology of the clavicle. This anomaly is defined as a discontinuity or cleft in the middle third of the clavicle that is caused by the nonunion of the two ossification centers (Gibson and Carroll, 1970; Lloyd–Roberts et al., 1975; Manashil and Laufer, 1979; Curraino and Herring, 2009). Thus, radiological findings in live subjects are characterized by clear separation in the middle portion of the clavicle, with the medial fragment positioned above the lateral fragment due to the action of muscle forces and the postural traction exerted by the weight of the upper limbs. The ends of the two bone segments are covered by cartilage and are often separated by fibrous tissue, and sclerotic closure of the medullary canal and the absence of the formation of a reactional bone callus are observed (Manashil and Laufer, 1979; Figueiredo et al., 2012).

Most studies have indicated that this lesion is caused by the pressure that is exerted upon the developing clavicle by the pulsating subclavian artery during intrauterine life (Lloyd–Roberts et al., 1975; Hirata et al., 1995). The right clavicle is the most affected site here, which is because the right subclavian artery is normally situated at a higher level than the left subclavian artery. However, clavicular pseudarthrosis on the left side is associated with relevant anatomical anomalies, such as dextrocardia, cervical ribs, or high vertically oriented upper ribs (Gibson and Carroll, 1970; Lloyd–Roberts et al., 1975; Beslikas et al., 2007; Curraino and Herring, 2009; Figueiredo et al., 2012). These anomalies can involve an aberrant origin and course of the subclavian artery that cause it to pass closer to the clavicle.

Bone tumors are also characterized by early osteosclerotic and osteolytic changes, and radiographically, the zones affected exhibit lucent areas (Freyschmidt, 2003). In any case, this bone lesions are clearly different to clavicle SGS01.

Finally, the clavicle is the most frequently fractured bone in the human skeleton. Clavicular fractures are not uncommon in children, especially before the age of 10 years. Such fractures account for $\sim$50% of all injuries to the shoulder region, and the middle of the clavicle is the primary site of fractures (Freyschmidt, 2003). It is possible that the neurovascular bundle become entrapped by the apposition of bone as consequence of a fracture occurred in childhood, and the callus may have been reabsorbed as a result of bone remodeling. Otherwise, the shaft of the clavicle is well aligned and this is a rare condition in ancient pathological human remains (Ortner, 2003). In adults, 70%–85% of all clavicular fractures involve the middle third of the shaft of the bone (Freyschmidt, 2003; Andermahr et al., 2007; Walters et al., 2010). These clavicular fractures commonly result in the formation of a large callus.

Clavicle SGS01 from Sulmona does not exhibit macroscopic, microscopic, or radiographic signs related to the pathological conditions described above. The macroscopic and radiographic observations of the clavicle revealed the absence of a lobular contour of the canal that would be expected to result from focal lesions, such as a stable fibroma or granuloma. We can reasonably state that the foramina and the connecting canal of clavicle SGS01 are not the result of pathogenetic mechanisms. The shape, size, and topographical orientation of the foramina and canal, however, do resemble the morphology of and would allow for the passage of the subclavian vessels.

Possible genesis of the anomaly. The unique combination of membranous and endochondral ossification that occurs in the human clavicle can at least partially explain the susceptibility of the clavicle to disturbance during development. Thus, the observed anomaly in clavicle SGS01 might have a pathogenesis of embryological–vascular origin. This variant might be related to a relatively higher anatomical position of the fetal vascular bundle, which would result in a blood vessel (the subclavian artery or vein) exerting pressure on the clavicle during development. This positioning would subject the clavicle to exaggerated venous or arterial pulsation in the region of the diaphysis, which can alter the normal processes of ossification (Scheuer and Black, 2004:250). This pressure might increase when the costoclavicular interval is narrowed by diverse processes that result in the compression of the vascular bundle by the adjacent structures as it passes through them. These processes can be classified as follows: (i) structural abnormalities, which can include congenital muscle anomalies and bony anomalies of the vertebrae, ribs or clavicle, for example, the presence of well-formed cervical ribs or a rudiment with a fibrous connection on the first rib or vertically disposed and elevated upper ribs; (ii) functional abnormalities, which can include abnormal positioning of the scapula or clavicle relative to the chest wall, and the overuse or nonphysiological use of the muscles of the shoulder girdle, which can result in hypertrophy of the scalene muscles; and (iii) post-traumatic abnormalities, which can include healed fractures of the ribs or clavicle and soft-tissue injuries of the scalene muscles or other supporting structures of the neck (Urschel and Kourlis, 2007; Abdul–Jabar et al., 2008; Rockwood and Matsen III, 2009; Ferrante, 2012; Klaassen et al., 2014). However, the last two processes (i.e., functional and post-traumatic abnormalities) seem to be more relevant during the post-natal life of an individual.

In any case, due to the absence of other skeletal elements that can be identified as belonging to the same individual, it has not been possible to conduct a more exhaustive study.

The sizes of the foramina and the canal of clavicle SGS01 are within the normal ranges of variation of the left subclavian artery in adult individuals (Testut, 1943; Kahraman et al., 2006; Coselli and Lemaire, 2008; Alsaif and Ramadan, 2010) and the left subclavian vein (Mitchell and Clark, 1979; Fortune and Feustel, 2003; Boon et al., 2007; Hurst, 2014). Therefore, two scenarios can be proposed for clavicle SGS01: (i) inclusion of the subclavian vein or (ii) inclusion of the subclavian artery. In scenario (i) the vessel and its tributaries would fit within the canal and pass through the foramina; the topographical position and diameter (Stickle and McFarlane,1997) of the external jugular vein match with the position and size of the superior foramen of the clavicle SGS01 (Fig. 6A). In scenario (ii), however, the subclavian artery would occupy the

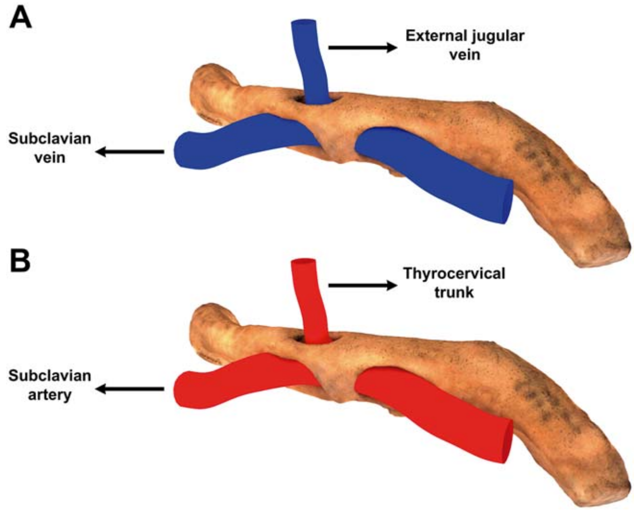

Fig. 6. Two scenarios that can be hypothesized to explain the anomaly observed in clavicle SGS01. **A**: Inclusion of the subclavian vein. In this case, the external jugular vein match with the position and size of the superior foramen. **B**: Inclusion of the subclavian artery. In this case, the thyrocervical trunk (the location of which corresponds topographically with the middle third of the clavicle) would have left from the superior foramen of the clavicle.

central canal and exit the two foramina on the anterior surface of the canal, while the thyrocervical trunk (the location of which corresponds topographically to the middle third of the clavicle) would pass through the superior foramen (Fig. 6B).

In either of these scenarios, any of these adjacent major blood vessels could be altered in terms of its angle relative to the horizontal axis of the clavicle and displaced 1–2 cm anteriorly and superiorly from its normal anatomical location during the development of the clavicle. In any case, variations of the origin and course of the subclavian artery and vein (including their branches) are reported in clinical cases (e.g., Saadeh and El-Sabban, 2005; Oguz et al., 2010; Reinhardt et al., 2011; Ali and Wase, 2012).

CONCLUSION

Based on the above considerations, the most probable diagnosis of the anomaly observed in clavicle SGS01 from Sulmona is consistent with a congenital anatomical variant that would have originated during fetal growth and resulted in the subclavian vein or artery remaining included during the process of the ossification of the clavicle. Thus, our case represents a new congenital anomaly that involves the clavicle and blood vessels.

AUTHOR CONTRIBUTIONS

Conceived the project: RD; collected the data: JV, VU and RD; analyzed and interpreted the data: JV, VU and RD; wrote the paper: JV and RD; created the Figures: JV.

CONFLICT OF INTEREST

None of the authors have any financial or personal relationships with other people or organizations that could inappropriately influence or bias this work.

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