FROM AN ATLAS OF GENERAL AFFECTIONS OF THE SKELETON

12. CRANIO-CLEIDO-DYSOSTOSIS

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This congenital condition is characterised by deficient formation of the clavicles with delayed and imperfect ossification of the cranium, associated in many cases with other anatomical errors. The first case of clavicular defect is said to have been reported by Martin (1765). One, with both clavicles and the skull affected, was reported in 1871 by Scheuthauer. Marie and Sainton (1898) named the condition hereditary cranio-cleido-dysostosis and called attention to irregularities in the dentition. For long it was thought that the changes were confined to bones that normally ossify in membrane but, in fact, bones preformed in cartilage are often affected.

In view of the widespread and variable abnormalities discovered in cases that might be regarded as belonging to this group, Rhinehart (1936) suggested the alternative title of mutational dysostosis—a suggestion that was supported by Soule (1946)—but this seems to be much too comprehensive a title. Three valuable reviews of the subject have been published by Fitzwilliams (1910), Fitchet (1929) and Soule (1946).

Hereditary and familial influences—Heredity undoubtedly plays an important part in the incidence. Stocks and Barrington (1925) found that the condition was inherited in more than half the cases they collected, namely in ninety-six of a total of 144. It has been traced through five generations (Soule 1946) but it is said as a rule to disappear after two or three generations. It may be inherited through either parent with about equal frequency. Soule, combining Fitchet’s figures with his own, found that in a total of 323 cases 198 were familial, these occurring in fifty-two families, while 125 cases were sporadic.

Sex—Both sexes are affected to an approximately equal extent.

Age—It may be discovered at any age. The cranial deficiencies may be noticed at birth. Fitzwilliams’ cases included a baby one month old and a woman of sixty years. The defective clavicles cause little if any disability and may easily escape notice for many years but nearly 70 per cent. of the reported cases were discovered before the age of twenty years.

Etiology—The cause of this primary error of development is entirely unknown. It is one of the conditions that Jansen (1921) attributed to increased intra-uterine pressure, but his theory has not been generally accepted. There is no doubt that the development of the clavicles must be disturbed at a very early stage of foetal life. It has been discovered in a twin, a girl, the other twin, a boy, being normal.

Distribution of the abnormalities—This shows considerable variation. The clavicular error is present almost without exception and is usually accompanied by deficiency of the cranium. Defects in the skull appear to be always symmetrical. As to the clavicles, one or both may be defective. Fitzwilliams found a unilateral defect in only six of sixty cases. Stocks and Barrington found bilateral defects in 82 per cent. of their cases; only two patients, both with typical changes in the skull, had normal clavicles. Other sites of developmental errors are the teeth, the mandible, the hands and feet, the pubis, the femoral necks and the neural arches. Paltauf (1912) seems to have been the first to note the gap in the pubic symphysis. Crouzon and Bouttier (1921) suggested that a case with deficient ossification of the pubis be labelled "forme cleido-crânio-pelvienne", while Latham (1945) proposed the term cranio-pubo-dysostosis for a case with normal clavicles.

Clinical signs—The striking features of a typical case are the slender build, the large head with small shrunken face, long neck, drooping shoulders and narrow chest. Growth of the whole skeleton is retarded and there may be a certain degree of dwarfism, but this is not a
marked feature as a rule. The mentality is normal. In at least one-third of the cases the skull shows well-marked frontal prominences separated by a median gutter. The parietal bones and sometimes the occipital bone may also form prominences, making six bosses in all on the skull (Stocks and Barrington 1925). The orbital ridges are well marked but the lower margins of the orbits are shrunken or even deficient. The anterior fontanelle is large and may never close completely. In some of the younger patients a much greater deficiency in the calvarium is seen. The eyes are rather far apart. The palate is high. A mild degree of hydrocephalus may be present. The maxillae are small so that the relatively large mandible may be prognathous. Delayed eruption, non-eruption and incomplete development of the permanent teeth are common. The temporary teeth erupt well and may be retained longer than normal; but when they are shed the retention of permanent teeth within the jaws may necessitate the wearing of dentures. Supernumerary permanent teeth are sometimes present. Dentigerous cysts may occur.

As a rule, the defects in the clavicles are easily felt. Sometimes there is no more than a kink in the middle of the bone or merely a diploe of the skin. The position of the shoulders —low and a little forward—and their abnormal mobility are no more than would be expected. Though the muscles may be defective in some anatomical details their power is not usually diminished. Many patients reach adult life entirely unaware of the defect in spite of hard manual work involving heavy lifting. Noticeable weakness of the shoulders and a tendency to undue fatigue are exceptional. When both clavicles are affected the shoulders can be approximated voluntarily in front of the chest to an abnormal degree and can be made to meet by gentle passive force. The scapulae may be small, somewhat deformed, rather winged and prominent, and more mobile than normal. Subluxation of the humeral head has been found in a few cases. The dislocation was complete in one case (Gross 1903), and could be easily completed by manipulation in another. We found both humeral heads subluxated downwards in a boy aged seven years. Bilateral subluxation of the radial heads has also been reported. Unusual length of the first finger is not uncommon. The fifth metacarpal may be shorter than normal. The terminal phalanges and the nails are short, particularly in the thumbs and great toes.

Other skeletal abnormalities have been found in individual cases. Postural defects and spinal curvature are common. Spina bifida occulta, often widespread in the spine, is of no clinical importance. Syringomyelias has been found as a complication. Widening of the symphysis pubis and deficient ossification of the pubic bones are not obvious clinically and even when sought are often not palpable. In younger patients the pubes are present, though partly or completely devoid of ossification. Coxa vara can be recognised by the usual signs. Other deformities that have been reported in individual cases are subluxation of a hip or a finger joint, and absence of the radius. In a case with deficiency of only one clavicle there was bilateral synostosis of the radius and ulna (Avery 1930).

**Radiographic appearances**—**Skull**—The membranous calvarium shows various degrees of imperfect ossification. The base is ossified normally. The sutures often fail to close normally. The anterior fontanelle is large and may never close; it may reach nearly to the level of the orbital ridges even in an adult. Occasionally there is a larger defect anteriorly, even in middle life. A fontanelle may be present posteriorly in both mastoid regions and also in the sphenoid. The mastoid itself may not be pneumatized (Salmon 1944). Wormian bones are seen in the occipital and posterior parietal regions. The frontal sinuses are often absent but occasionally they are disproportionately large, the other sinuses being small. In extreme cases there may be no ossification whatever in most of the vault. In one of our patients, aged three years, the two parietals were apparently unossified. The pituitary fossa may be small but it shows no constant change. The maxillae are hypoplastic but the mandible is of normal dimensions: fusion at the mandibular symphysis may be delayed or even fail to occur. There was no sign of fusion in a boy aged eight years reported by Ingham (1947). The mental tubercles
may be unusually long. The nasal, lachrymal and malar bones may be incomplete or absent (Salmon 1944). In some cases ossification of the skull is normal.

Clavicles—Stocks and Barrington (1925) found that the commonest defect was absence of the outer end of the clavicle, the sternal half being present. The next commonest condition was the presence of two separate fragments for each clavicle (28.2 per cent.—but this figure seems unduly low). The inner fragment was usually the larger of the two: the outer may not reach the acromion. The least common defect was absence of the sternal end with the acromial end present. Complete absence of both clavicles was uncommon (8.1 per cent.), and absence of one clavicle only was exceptional. These findings are supported, more or less, by other authors. Stocks and Barrington found pseudarthrosis between the two fragments in only three cases: the adjacent ends of the fragments in such cases may be enlarged or they may overlap. In only two of their cases, both with typical skull changes, were the clavicles normal. Nettlesheim (1926) reported the case of a woman aged twenty-nine years with the left clavicle in three pieces and the right in two. Everley Jones (1937) rightly called attention to the need for care in examining radiographs since a clavicular fragment may easily be overlooked. In ten cases with clavicular defects this author found both clavicles represented by two fragments in all but one: in this there were two clavicular fragments on one side and only the sternal portion present on the other. The bones of the limbs generally are rather slender. In many of the recorded cases it seems probable that the pelvis and hips were not specially examined, so that the frequency of abnormalities in this region is uncertain.

Pubes—In most cases no reference is made to the condition of the pubes. In the author's small series of twelve cases, ten, varying in age from three to eighteen years, showed deficient ossification of the pubis, the deficiency being bilateral in all. In the other case—an adult woman—the pubes were well ossified; but her two affected children both showed defects of the pubes as well as other signs of dysostosis. The degree of deficiency was found to vary. In three patients there was complete absence of ossification in the pubes, both body and rami. The oldest patient of this group was a boy aged fifteen years who showed some stippling in the pubic part of the acetabulum. In six of the remaining seven cases there was a fragment of bone of varying size in the horizontal ramus, the body and descending ramus being completely unossified. Ossification of the pubis is only delayed; it occurs eventually, though often incompletely. The inferior ramus of the ischium shares in the delayed and defective ossification. The symphysis may remain unusually wide with an irregular boundary on each side. In such cases the fusion of the conjoint rami may be incomplete and their thickness considerably reduced. The case of a woman aged twenty-four years with these changes in the pelvis, and gross deficiencies in the clavicles, was reported by Steel and Whitaker (1937). Imperfect or delayed ossification of the pubes is not, however, invariably found in cases showing other clear signs of the condition. For instance, Fitchet (1929) published six cases in three generations of a family, in all of which the pubes were normal and there was no coxa vara. The pelvic ring may be reduced in size but seldom to a sufficient degree to cause trouble in childbirth. The sacro-iliac joints may be increased in width.

Coxa vara—In the author's series of eleven cases there was coxa vara in five—bilateral in three, unilateral in two. Both clavicles were deficient in four of these patients: the fifth had unilateral coxa vara and a defect of one clavicle, both on the same side of the body, while failure of ossification of the pubis was present on both sides. The type of coxa vara seems to vary. Klar (1906), the first to record this deformity, called the coxa vara in his case "congenital." But Ollerenshaw (1938) considered this type unusual. In his opinion the deformity occurred in the upper part of the femoral shaft and he had not seen coxa vara of the infantile type in the "many well-marked cases" of cranio-ileo-dysostosis he had seen. The author's experience differs from this, for in every case with coxa vara (a total of eight abnormal hips) the deformity was invariably of the infantile or cervical variety (Fairbank 1927, 1928). Soule (1946) said that infantile coxa vara was common. In Crouzon and
Bouttier’s case (1921) the acetabula were deformed and the mobility of the hip joints was much increased.

**Spine**—Failure of union of the neural arches is common and may involve several vertebrae in the dorsal and lumbar regions. In one case we found spina bifida occulta from the sixth cervical to the sixth dorsal vertebra. In younger patients the vertebral bodies are inclined to be biconvex and the discs biconcave; in older patients they may show some reduction in depth. Various other congenital deformities of the spine, including half vertebrae and incomplete or complete absence of the lower part of the sacrum and coccyx, have been reported; but such exceptional findings are of little interest and of no diagnostic significance. Eltorm (1945) reported a curious case, a woman aged fifty-two years, with the dorsal bodies wedged *posteriorly* and showing defective ossification. The ribs may slope downwards to a greater degree than usual. The sternum may be of peculiar shape: failure of the manubrium to ossify has been recorded.

**Hands and feet**—In the hands and feet, various abnormalities have been found, the most constant and curious being the presence of epiphyses at both ends of the metacarpals and metatarsals, particularly of the second and fifth, and an abnormally long second metacarpal. The epiphysis which occurs at the base of the second metacarpal is strikingly large. The ungual tuberosities are poorly developed or absent, the terminal phalanges being short and pointed, particularly in the thumb and great toe (Brailsford 1935). The intermediate phalanges may be small; they may show curious ossification or even be absent. Ossification of the carpus may be delayed. The calcaneum may be short.

**Complications**—Pressure on the brachial plexus, relieved by removal of the outer fragment of the clavicle, was reported by Poynton and Davies (1914). One patient who complained of pain and numbness in the ulnar area, accompanied by cyanosis, was treated by bone-grafting operations on both clavicles (Everley Jones 1937). Ollerenshaw (1938) reported two cases, a brother and sister, with calcification in the skin and soft tissues. Syringomyelia has been mentioned already as a rare complication.

**Pathology**—There is no abnormality in the bone of the calvarium and clavicles except the limitation of its distribution. The base of the skull is said to be narrowed, especially in the middle portion. The cranial bones are thickened where bosses occur. The muscles acting on the shoulder girdle show a number of abnormalities varying with the type of clavicular deficiency (Fitzwilliams 1910, Everley Jones 1937). Their relative frequency corresponds broadly with that of the various deficiencies of the clavicle. The commonest are absence of the clavicular portion of the trapezius and the anterior fibres of the deltoid. Occasionally the sterno-mastoid and pectoralis major are deficient, but the clavicular parts of these muscles are affected only when the sternal part of the clavicle is very small or completely absent—a rare occurrence. When the sternal portion alone is present the bone is prolonged outwards by a ligament or fibrous band which in most cases passes to the coracoid and not to the acromion. The ligament may even be attached to the glenoid or to a rib (Fitzwilliams): it is regarded as the costo-coracoid membrane. When there are two fragments these are usually united by a ligament.

**Diagnosis**—This should present no difficulty. Absence of ossification of the pubis may be of diagnostic value. If found by accident it may lead to the discovery of deficiencies in the skull and clavicles. In a young patient showing pseudarthrosis of a clavicle, with thickening of the fragments, and without obvious deficiency in the skull, radiographic examination of the pelvis might remove any doubts as to the case being due to an error of development and not to trauma. Evans (1924) reported the case of an infant with an absent tibia and complete absence of ossification in the femoral head on the same side and in the pubis on both sides. The condition of the clavicles is not mentioned but the skull appears to have been normal.
REFERENCES

Evans, E. Laming (1924): Proceedings of the Royal Society of Medicine (Orthopaedic Section), 17, 53.

CASE 23
CRANIO-CLEIDO-DYSOSTOSIS

(Fig. 66.) Tracing of the radiograph published by Steel and Whitaker showing the wide symphysis and imperfect ossification of the pubes and conjoint rami in a woman of twenty-four years. There were deficiencies in the skull, and absence of the outer two-thirds of both clavicles.

Fig. 66.
CASE 24—CRANIO-CLEIDO-DYSOSTOSIS

(Figs. 67-73.) Male, aged seven years. One of a family of seven children, the others being normal. Has always presented the same general appearance with large head and narrow shoulders. Typical changes in the skull, clavicles, pubes, hands and feet. Anterior and temporo-parietal fontanelles patent and membranous; frontal and parietal eminences prominent. Marked frontal fissure. No sign of frontal sinuses which should be visible at this age. Wormian bones in the occipital region. Lambdoid suture closed. Teeth very irregular. On extraction of carious temporary teeth there was practically no absorption of the roots. The shoulders can be "bunched together." The right shoulder droops more than the left; radiographs showed that the humeral head was subluxated downwards.
Case 24. Chest and shoulders showing the narrow thorax. The right clavicle is represented by two fragments and the left clavicle is deficient in its outer part where it fails to reach the acromion.

Case 24. Hand showing delayed ossification of the carpus, epiphyses at the bases of the second and fifth metacarpals, and abnormal shape of the intermediate and terminal phalanges.

Case 24. Feet showing additional epiphyses at the bases of the second metatarsals. The shape of the internal cuneiforms and of the phalanges, particularly of the great toes, is abnormal.
Case 24. Pelvis and hips showing absence of ossification in the bodies and descending rami of the pubes, and delayed ossification in the inferior rami of the ischia. The horizontal pubic rami are represented by oval fragments of bone.

**CASE 25—CRANIO-CLEIDO-DYSOSTOSIS**

(Fig. 74.) Female with bilateral clavicular dysostosis, each clavicle being represented by two fragments. Skull apparently normal (but not radiographed). Pubes ossified but distinctly less dense than the rest of the pelvis. No coxa vara. The width of the symphysis is approximately normal. The patient had three children, two affected by dysostosis: both had bilateral clavicular dysostosis, all four clavicles being in two fragments. In the elder child, a boy aged twelve years, there was no ossification of the pubic body or descending ramus on either side, whereas the horizontal rami consisted of bone; there was coxa vara on the right side only; the only abnormalities in the skull were absence of the frontal sinuses and presence of Wormian bones in the occipital bone. The younger child, a girl, showed similar bilateral delayed ossification of the pubis but no coxa vara.
CASE 26—CRANIO-CLEIDO-DYSOSTOSIS
(Figs. 75 and 76.) Female, aged six years. Always weak on legs: gait waddling. Lordosis present. Skull generally well ossified. Wormian bones in the occipital region. Bilateral division of the clavicle into two fragments. Bilateral coxa vara, which radiographs showed to be of the cervical or infantile type. Subtrochanteric osteotomy performed on both femora. The body and descending ramus of the pubis, and the ascending or inferior ramus of the ischium, are unossified on both sides. The horizontal rami of the pubes are ossified. On palpation no deficiency can be felt in the pubic region. Additional epiphyses and other changes present in the hands. The terminal phalanges of the toes, particularly of the great toe, are typical.

![Fig. 75](image-url)

Case 26. Thorax and shoulders showing both clavicles in two fragments, the outer being smaller and not making contact with the acromion.

![Fig. 76](image-url)

Case 26. Pelvis and hips showing absence of ossification in the bodies of the pubes and the conjoint rami, and typical infantile coxa vara of both femora. Note that the horizontal rami of the pubes are ossified.
CASE 27—CRANIO-CLEIDO-DYSOSTOSIS

(Figs. 77-80.) Male, aged three years. No abnormality noticed by the parents. Fourth of four children, the others and the parents being normal. Gross deficiency in the calvarium; the parietals show little if any signs of ossification; anterior fontanelle very large. Two fragments for each clavicle. Epiphyses at both ends of all metacarpals. Ossification of carpus delayed. Both pubes completely devoid of bone. No coxa vara. Delayed fusion of mandibular symphysis and of neural arches of the spine. The density of most bones is below normal. (Under Sir L. Barrington-Ward.)

Fig. 77

Case 27. Skull showing enormous fontanelle, limited union of the two halves of the frontal bone, and absence of fusion at the mandibular symphysis (Fig. 77). In the lateral view note the gross deficiency in ossification particularly of the parietals, and many Wormian bones in the occipital (Fig. 78).

Fig. 78

Fig. 79

Case 27. Pelvis showing complete absence of ossification in the pubes and inferior rami of the ischia (Fig. 79). The lower forearm and hand (Fig. 80) shows osteoporosis of the bones, double epiphyses for all metacarpals, and a curious shape of many phalanges.