

CLINICAL FEATURES OF EMBRYOLOGICAL FAILURES

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INTRODUCTION

Swanson (1968) et al.¹⁾ proposed the simplest classification and nomenclature of congenital anomalies of the hand based on embryological failure, and this classification has been adopted by the American Society for Surgery of the Hand, the International Federation of Hand Societies, and the International Society for Prosthetics and Orthotics.

In this classification, the failure of formation of parts (arrest of development) is divided into two types: transverse and longitudinal. The transverse defects include all so-called congenital amputations except for amputation with the constriction band syndrome. Longitudinal deficiencies include all deficiencies that are not in the transverse category. The failure of differentiation (separation) of parts is classified into that of shoulder, arm, forearm, and hand. The anomalies of the hand are classified into carpal, metacarpal, and digital, and the digital anomalies are further classified into deformities, symphalangism, syndactyly (simple and complicated), and contracture secondary to failure of differentiation of muscles, ligaments, and capsular structures. The other type of anomalies are duplication, overgrowth (gigantism), undergrowth (hypoplasia), congenital constriction band syndrome, and generalized skeletal abnormalities.

The worldwide adoption of such a uniform classification is valuable for monitoring the congenital anomalies of the hand, and is of fundamental help in the research of the causative factors, preventative measures, and methods and outcome of treatment. It also permits comparisons of incidence between different areas and different countries. The embryologic failure, however, is not clear, and we have found that etiologic groupings made according to this classification, in some cases, are difficult and misleading.

Since 1976, I have had a great interest in the clinical similarity of cases otherwise distinguishable by appearance such as typical cleft hand and webbing of normal fingers, and have reported a few conclusions.²⁻⁴⁾

CLINICAL FEATURES

Typical cleft hand

In many cases of typical cleft hand, I found that the following clinical features represent the union of the digital rays: (1) When the metacarpal of the missing finger was present, the corresponding proximal phalanx was thickened. In cases where the metacarpal was absent the metacarpals on either side of the cleft were usually thickened. (2) When two or more digits were present on the radial and/or ulnar side, the remaining neighboring digits were often webbed.

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(3) Most cases with a retained single digit on the radial side, suggesting a thumb, had an additional interposing bone in the interphalangeal joint, and the first metacarpal of the digit had two epiphyses on both the proximal and distal ends. (4) Some of these cases had broad, perforated distal phalanges. (5) Some of the distal phalanges on the side of the cleft were duck-bill shaped. (6) In some cases of cleft hand in which the third metacarpal was present, arteriograms showed that each hand had three arteries to the ring finger. (7) In almost all patients with a cleft hand missing only the middle finger, the main fibers of the extensor digitorum communis tendon of the middle finger ran to the dorsum of the proximal phalanges of the ring finger with some branching out to the radial side, there were two extensor communis tendons on the dorsum of the proximal phalanges of the ring finger. (8) Syndactyly of the opposite hand and/or feet was not rare, and patients with webbing of the normal fingers were often found in the same family.

Typical cleft hand and webbing of normal fingers

At the beginning of the present study, some intermediate cases between the two anomalies, cleft hand and syndactyly, were encountered. Some could not be called cleft hand, and others could not be called syndactyly. However, as these two groups of cases had the same radiological features, it was difficult to classify them into separate categories.

Webbing of normal fingers and typical cleft hand had the following clinical similarities: (1) In the majority of cases of syndactyly and cleft hand the malformation was bilateral and also occurred in the feet. (2) In most cases of syndactyly the middle and ring fingers were webbed. In the cases of cleft hand the middle finger was usually absent. (3) Unaffected digits were fully developed except for the middle phalanges of the little and index fingers. (4) Both syndactyly and cleft hand were often hereditary, and these anomalies were transmitted as an autosomal dominant phenotype. (5) Brachymesophalangy 5 (shortening of the middle phalanx of the little finger) was frequently found (about 50%) in both syndactyly and cleft hand, and brachymesophalangy 2 (shortening of the middle phalanges of the index finger) was also found.

These similarities of the clinical features may show that these two seemingly different anomalies have the same pathogenesis, and that typical cleft hand is a result of the union of digital rays.

Typical cleft hand and failure of formation of parts

There were many differences between cleft hand and radial ray deficiencies as follows: (1) In radial ray deficiencies, the thumb was sometimes present even when the proximal bones were absent; while in cleft hand, the proximal bone was always present whenever the corresponding distal bone was present. (2) In radial ray deficiencies, the neighbouring metacarpals were never thickened, and the remaining digits were never webbed. (3) Carpal bones in some cases of cleft hand were sometimes fused but were always present. In radial ray deficiencies, some radial carpal bones were missing or hypoplastic.

The differences between typical and atypical cleft hand were as follows: (1) The digital rays remaining in the atypical cleft hand were markedly hypoplastic. (2) Many cases of atypical cleft hand had small finger nubbins representing missing digits in the central parts of the hand.

These differences of clinical features between typical cleft hand and failure of formation suggest that typical cleft hand is not a result of the failure of formation.

Syndactyly and brachysyndactyly

There were many differences between webbing of normal fingers and webbing of short fingers (brachysyndactyly): (1) The affected hand in brachysyndactyly was unilateral and smaller than a normal hand. In contrast, in syndactyly, both hands were often affected, and the bony formation

CLINICAL FEATURES OF EMBRYOLOGICAL FAILURES

of the phalanges were normal except for the middle phalanx. (2) Complications with foot anomalies were rarely found in brachysyndactyly. (3) Union of the phalangeal bones with neighboring digits was never seen in brachysyndactyly. (4) All cases of brachysyndactyly were sporadic.

These differences suggest that the pathogenesis of these two anomalies with webbing of the digital rays is different.

Brachysyndactyly and atypical cleft hand

Brachysyndactyly and atypical cleft hand had the following similarities, and these features were similar to congenital amputation by failure of formation: (1) The affected hand was smaller than the unaffected hand. (2) The malformation, in almost all cases, was unilateral and feet were normal. (3) Unilateral absence of the pectoral muscles was often found. (4) All cases were sporadic and not hereditary.

These findings may show that brachysyndactyly is a result of failure of formation as is atypical cleft hand.

Polydactyly of the thumb

Polydactyly of the thumb had some characteristic features: (1) Most cases were sporadic, but some of them were inherited. (2) In some cases of polydactyly of the thumb with triphalangism, an opposable triphalangial thumb was found in the opposite hand. (3) The complication of syndactyly of the toes was more common than polydactyly of the foot.

These complications suggest that the critical period of polydactyly of the thumb is later than the critical period of syndactyly, and that the two anomalies, syndactyly and polydactyly of the thumb, might have the same pathogenesis because the hand plate develops a little earlier than the foot plate.

Cleft hand and polydactyly

There were some cases of central ray polydactyly suggesting a close relationship between the typical cleft hand and the webbing of normal fingers.

The arteriogram in one case clearly showed that the two central fingers were the result of separation of the middle finger. Most fibres of the flexor digitorum tendons of the middle finger, in this case, were directed toward the ulnar finger, and the extensor communis tendon branched into two parts directed to both the ulnar and radial fingers.

These findings in the cases of central polydactyly in one hand and cleft hand in the other suggest how the typical cleft hand is formed prenatally.

Other associated congenital anomalies

1) Associated foot anomalies

There were some interesting cases in which other combinations such as syndactyly with polydactyly or cleft foot, cleft hand with syndactyly or polydactyly, and polydactyly with syndactyly or cleft foot, were seen. I found no cases of dysplastic or aplastic thumb, brachysyndactyly or transverse deficiency (including atypical cleft hand) associated with polydactyly, cleft foot or syndactyly of the foot.

These complications of the foot suggest that the same pathogenesis might be responsible for the formation of cleft hand, polydactyly, and syndactyly, and that the critical period of these anomalies is the same.

2) Other associated anomalies

Anomalies of the internal organs, except post-axial polydactyly such as Ellis van Creveld syndrome, were associated with anomalies of the thumb, that is, dysplastic or aplastic thumb and

polydactyly of the thumb. Cleft lip and cleft palate were associated with syndactyly, cleft hand, constriction band syndrome and polydactyly of the thumb. Pectoral muscle anomalies were found not only with brachysyndactyly (Poland's syndrome) but also in the cases of congenital amputation by failure of formation of parts, radial ray deficiency, and polydactyly of the thumb.

Most authorities accept that combined anomalies are the result of genetic or environmental factors interfering with parts developing in the same critical embryonic period.⁵⁾ If this hypothesis is right, (1) the critical period of radial ray deficiency may be earlier than the period of webbing or union of digital rays, and (2) the critical period of webbing or union of digital rays may be a little earlier than the period of mesenchymal condensation, because pectoral muscle anomalies are found only in the cases of failure of formation from the level of the metacarpophalangeal joint and in almost all cases of brachysyndactyly, which may be a result of partial mesenchymal necrosis. (3) The critical period of polydactyly of the thumb may extend over a relatively long period.

VASCULAR PATTERN IN THE FOREARM⁶⁾

1) Radial ray deficiencies

a. Hypoplasia and aplasia of the radius

The major findings were aplasia or hypoplasia of the radial artery and persistence of the median artery. Aplasia was seen in two of the four cases, and in the other two cases where the thumb formation was relatively good, the radial artery was recognized.

b. Hypoplasia of the thumb

The radial artery could not be found in five out of seven cases, of hypoplasia of the thumb and in the other two cases it was dysplastic. The median artery was also persistent in all cases.

2) Ulnar ray deficiencies

In both cases of hypoplasia and aplasia of the ulna, the radial artery was not seen. The radial artery was also not seen in two of the three cases of failure of one or two ulnar digital ray(s), and in the other case the median artery was persistent.

3) Typical cleft hand

There was a well-formed radial artery in all 14 cases of typical cleft hand. One patient had a typical cleft hand on one side and a one-digit hand on the other side. The one-digit hand did not have radial artery.

4) Webbing of normal fingers

There was a well-formed radial artery in all 20 cases of syndactyly (15 cases were syndactyly between the middle and ring fingers, and five cases were syndactyly between the ring and little fingers).

5) Polydactyly of the thumb

All 22 cases of polydactyly of the thumb, except for one case with a slightly hypoplastic radial artery had a well-formed radial artery.

6) Congenital constriction band syndrome

All six cases of congenital constriction band syndrome had a well-formed radial artery.

7) Brachysyndactyly

In one of the six cases of brachysyndactyly, the radial artery was missing. The other five cases had a well-formed radial artery.

These complicated arterial anomalies in the forearm suggest that the period of formation of the radial artery is the same as the critical period of radial and ulnar deficiencies including the hypoplastic thumb, and this critical period might be earlier than the critical period of typical

CLINICAL FEATURES OF EMBRYOLOGICAL FAILURES

cleft hand, syndactyly, polydactyly, and constriction band syndrome.

HAND PATTERN PROFILE⁷⁾

The graphic technique of the hand pattern profile, to divide the bone length on the affected hand by the bone length on the unaffected side or by the Japanese standard in bilateral cases, can be used to clarify the embryologic failure.

Metacarpal pattern profile

The metacarpal pattern profile of several congenital anomalies of the hand were compared. There was an obvious difference in metacarpal pattern between typical cleft hand, syndactyly, and constriction band syndrome, and brachysyndactyly and congenital amputation by failure of formation, including atypical cleft hand. The graphic metacarpal pattern profiles showed that in typical cleft hand, syndactyly, and constriction band syndrome, the metacarpal length is almost normal, but in brachysyndactyly and failure of formation, the metacarpal length is shortened.

Typical and atypical cleft hand

In the typical cleft hand, if the third metacarpal was present, the proximal phalanx on the ring finger was longer than normal, and if the third metacarpal was lost, the fourth metacarpal was longer than normal. In the case of only one digit remaining on the radial side, the first metacarpal was more than 50% longer than the standard. In the atypical cleft hand, all metacarpals and phalanges were shorter than those on the unaffected side.

Webbing of normal fingers

All metacarpals and phalanges of 26 cases (35 hands), except the middle phalanges of the little finger, were as long as those on the unaffected side or the Japanese standard.

Brachysyndactyly

Shortening of the middle phalanges was a prominent feature, and all metacarpals and phalanges were also shortened.

Hand pattern profiles revealed that digital fusion is a distinctive feature of the typical cleft hand, but is not found in the atypical cleft hand, and that atypical cleft hand is closely connected with brachysyndactyly.

DERMATOGLYPHICS⁸⁾*Axial triradius*

Characteristic dermatoglyphic findings were seen in several congenital hand anomalies. The position of the axial triradius is an important landmark in trying to imagine the critical period, and if the axial triradius is absent or distally displaced, the mesenchyme in the hand plate must be impaired (partial necrosis of the mesenchyme).

1) Radial ray deficiencies

a) Hypoplasia and aplasia of the radius

The axial triradius was absent in seven of the eight hands in six cases, but in one hand it was situated in the normal position. In the hand in which the axial triradius was situated in the normal position, hypoplasia of the thumb was not found.

b) Hypoplasia and aplasia of the thumb

The axial triradius was absent in four hands and distally displaced by more than 30% from the wrist crease in 10 out of 16 hands in 11 cases. The axial triradius was situated in the normal position in only two hands (29.7% and 18.5%, respectively).

2) Ulnar ray deficiencies

a) Hypoplasia and aplasia of the ulna

The axial triradius was absent in two hands in two cases of hypoplasia and aplasia of the ulna.

b) Ulnar digital ray(s) defect

The axial triradius was absent in three hands in three cases, and distally displaced in three hands of three cases, 69.0%, 63.5%, and 47.6% from the wrist crease, respectively.

c) Dysplasia of the fourth digit

The axial triradius was situated 33.8% distally from the wrist crease.

3) Webbing of the normal fingers

The axial triradius was situated in the normal position in all 22 hands in 16 cases.

4) Synostosis between the fourth and fifth metacarpals

The axial triradius was situated normally in all three hands in two cases: 13.5%, 13.5%, and 12.5%, respectively.

5) Typical cleft hand

The axial triradius was situated in the normal position, less than 20% from the wrist crease, in 21 out of 24 hands in 16 cases; In the other three hands, it was situated less than 30% from the wrist crease: 21.2%, 22.8%, and 29.3%, respectively: but in the case that had a typical cleft hand on one side and a one-digit hand on the other side, the axial triradius was absent in the one-digit hand.

These dermatoglyphics show that (1) the critical period of the radial or ulnar ray is earlier than that of webbing or union of the digits. (2) The critical period of congenital amputation from the level distal to the metacarpophalangeal joint is later than that of webbing or union of the digits. (3) The critical period of brachysyndactyly is a little earlier than that of congenital amputation from the level of the metacarpophalangeal joint. (4) There is very little impairment of the mesenchyme in webbing of normal fingers and typical cleft hand.

Digital triradius

Absence or fusion of the digital triradius, which represents webbing or union of digital rays, was seen in brachysyndactyly and syndactyly, and in some cases of congenital amputation by failure of formation, but in the case of amputation by constriction band syndrome no abnormalities of the digital triradius were found. These findings suggest the similarity between congenital amputation by failure of formation and brachysyndactyly.

DISCUSSION

Clinical features, vascular pattern, hand pattern profile and dermatoglyphics make clear that cleft hand may not be the result of failure of formation, and that the union of the digital rays may be an embryonic failure.

The critical period of radial and ulnar ray deficiency may be earlier than the period of webbing or union of the digital rays and formation of phalangeal bones (mesenchymal condensation).

The critical period for transverse deficiency (transverse failure of formation of parts) may extend throughout the period of development of the limb buds. The earliest case is amelia, and the

CLINICAL FEATURES OF EMBRYOLOGICAL FAILURES

latest is aphalangia limited to the distal parts of one or two digits.

If partial necrosis of mesenchymal tissues occurs and regeneration follows, phocomelia, radial deficiency, floating thumb, and brachysyndactyly may result.

The critical period of webbing or union of digital rays may be a little earlier than the period of mesenchymal condensation, because pectoral muscle anomalies are found in almost all cases of brachysyndactyly, which may be a result of partial mesenchymal necrosis followed by regeneration, and in amputation only from the level of the metacarpophalangeal joint including the atypical cleft hand.

The critical period of webbing or union of digital rays may be the same as the period of formation of metacarpal and proximal phalangeal bones, and the period of formation of pectoral muscle anomaly.

The critical period of polydactyly of the thumb may be relatively long. The earliest part of the period is the same as the critical period of formation of dysplastic thumb, but the later part is a little after the critical period of webbing or union of the digital rays, because association with syndactyly of the foot, for which the developmental phase is a little later than that of the hand, is more common than that with polydactyly of the foot; and extension and involution of the apical ectodermal ridge on the prexial border are usually later than that in the center.

The critical period of webbing or union of the digital rays may be very brief, and in the same period, cleft hand may be formed as a result of union of the digital rays.

If necrosis of the mesenchymal tissue is the dominant feature in the formation of syndactyly and typical cleft hand, these hand anomalies would be accompanied by pectoral muscle anomalies as are brachysyndactyly or congenital amputation by failure of formation. However, I found only one case of 196 cases of syndactyly or typical cleft hand that was accompanied by pectoral muscle anomalies.

The hand pattern profile and dermatoglyphics clearly show that the impairment of mesenchymal tissue plays the leading role in the formation of such anomalies as radial or ulnar deficiency, congenital amputation by failure of formation, and brachysyndactyly, and that impairment of mesenchymal tissue may be slight in webbing of normal fingers and cleft hand.

Dermatoglyphics clearly show that the critical period of radial or ulnar ray is earlier than that of webbing or union of the digits, and that the critical period of congenital amputation from the level distal to the metacarpophalangeal joint is later than that of webbing or union of the digits.

The critical period of syndactyly and cleft hand is the same as that of brachysyndactyly.

CONCLUSION

There are three types of congenital anomalies: the first is abnormality of the number of digits, including polydactyly, syndactyly, and oligodactyly (cleft hand); the second is the anomaly of formation, including radial or ulnar deficiency, congenital amputation, and brachysyndactyly; and the third is the constriction band syndrome, which is formed after mesenchymal condensation.

The following classification made on the basis of embryological failure, is proposed:

1. Failure of formation of parts (caused by the necrosis or disorder of mesenchymal tissue)
 - a. Regeneration (+)

Phocomelia, radial or ulnar ray deficiency with relatively good digits, floating thumb, and brachysyndactyly

- b. Regeneration (—)

Terminal transverse deficiency, i.e., amelia, adactylia, etc., and missing thumb

2. Failure of induction of digital rays (caused by abnormal distribution of mesenchyme; abnormality of the apical ectodermal ridge)
 - a. Impairment of mesenchymal tissues (rare)
Syndactyly (of normal fingers), central polydactyly and typical cleft hand, and most cases of duplicated thumb and opposable triphalangeal thumb
 - b. Impairment of mesenchymal tissues (moderate or severe)
Complicated syndactyly, some cases of duplicated thumb and nonopposable triphalangeal thumb
3. Congenital constriction band syndrome (tissue necrosis after mesenchymal condensation)
Constriction ring, congenital amputation by constriction band, and acrosyndactyly.
Three other categories may be added:
4. Generalized skeletal abnormalities
5. Failure of differentiation
Synostosis (skeletal fusions at joint spaces) and contracture of the soft tissues, which are included in failure of differentiation in Swanson's classification
6. Overgrowth or undergrowth
Macroductyly and any type of abnormal growth that can not be included in the failure of formation of parts at present.

At present, however, the pathogenesis is not clear in many cases of anomalies of the hand, and it may be impossible to explain the pathogenesis perfectly in the future. There are many cases, clinically, in which necrosis of the mesenchymal tissues and abnormal distribution of the mesenchyme are combined, and we can not imagine which plays the leading part, necrosis or abnormal distribution of the mesenchyme. The classification on the basis of embryologic failure is ideal, but it may be unrealistic. However, the classification is indispensable in enabling comparisons to be drawn and incidence rates to be established. I clearly showed that the cleft hand could not be included in the failure of formation, and that brachysyndactyly should be included in the failure of formation.

In conclusion, I propose that Swanson's classification should be modified as follows: 1) Cleft hand should be regarded as failure of differentiation, hand, digital, syndactyly, and cleft hand complex.⁹⁾ 2) Brachysyndactyly should be regarded as failure of formation, transverse, brachydactyly, and webbed. 3) Atypical cleft hand and congenital amputation by failure of formation should be regarded as failure of formation, transverse, brachydactyly, and web free.

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