Upper-extremity phocomelia reexamined: A longitudinal dysplasia

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Upper-Extremity Phocomelia Reexamined: A Longitudinal Dysplasia

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Investigation performed at Texas Scottish Rite Hospital, Dallas, Texas, and Shriners Hospital for Children, St. Louis, Missouri

Background: In contrast to longitudinal deficiencies, phocomelia is considered a transverse, intercalated segmental dysplasia. Most patients demonstrate severe, but not otherwise classifiable, upper-extremity deformities, which usually cannot be placed into one of three previously described phocomelia groups. Additionally, these phocomelic extremities do not demonstrate true segmental deficits; the limb is also abnormal proximal and distal to the segmental defect. The purpose of this investigation was to present evidence that upper-extremity abnormalities in patients previously diagnosed as having phocomelia in fact represent a proximal continuum of radial or ulnar longitudinal dysplasia.

Methods: The charts and radiographs of forty-one patients (sixty extremities) diagnosed as having upper-extremity phocomelia were reviewed retrospectively. On the basis of the findings on the radiographs, the disorders were categorized into three groups: (1) proximal radial longitudinal dysplasia, which was characterized by an absent proximal part of the humerus, a nearly normal distal part of the humerus, a completely absent radius, and a radial-sided hand dysplasia; (2) proximal ulnar longitudinal dysplasia, characterized by a short one-bone upper extremity that bifurcated distally and by severe hand abnormalities compatible with ulnar dysplasia; and (3) severe combined dysplasia, with type A characterized by an absence of the forearm segment (i.e., the radius and ulna) and type B characterized by absence of the arm and forearm (i.e., the hand attached to the thorax).

Results: Twenty-nine limbs in sixteen patients could be classified as having proximal radial longitudinal dysplasia. Systemic medical conditions such as thrombocytopenia-absent radius syndrome were common in those patients, but additional musculoskeletal conditions were rare. Twenty limbs in seventeen patients could be classified as having proximal ulnar longitudinal dysplasia. Associated musculoskeletal abnormalities, such as proximal femoral focal deficiency, were common in those patients. Eleven limbs in ten patients were identified as having severe combined dysplasia, which was type A in seven of them and type B in four. Four patients with severe combined dysplasia had congenital cardiac anomalies, and four had associated musculoskeletal abnormalities. Three of the four patients with the type-B disorder had a contralateral ulnar longitudinal dysplasia.

Conclusions: We propose that cases previously classified as upper-extremity phocomelia represent a spectrum of severe longitudinal dysplasia, as none of the sixty extremities that we studied demonstrated a true intercalary deficiency. These findings have both developmental and genetic implications.

Level of Evidence: Diagnostic Level II. See Instructions to Authors for a complete description of levels of evidence.
rach. In type III, the distal type, the hand is attached to the humerus. Patients categorized as having one of these three types of phocomelia may have a very rare syndromic association or a spontaneous birth defect. More commonly, patients diagnosed as having phocomelia demonstrate severe, but not otherwise classifiable, upper-extremity deformities that usually cannot be placed into one of the above three groups. Additionally, these extremities do not demonstrate true segmental deficits; the limb is abnormal proximal and distal to the segmental defect, suggesting a longitudinal dysplasia.

The purpose of this investigation was to reevaluate the findings in patients previously diagnosed as having upper-extremity phocomelia and determine whether their disorder should be classified as a severe form of longitudinal dysplasia—i.e., a failure of formation along the longitudinal axis. Specifically, it was our hypothesis that these patients could be classified as a severe form of longitudinal dysplasia.

The contralateral extremity of each patient was assessed with a review of the medical records and the radiographs. In most cases, the contralateral extremity did not have phocomelia but was abnormal, usually presenting with a longitudinal deficiency. These limbs were classified with use of standard classification systems; the Bayne and Klug classification system was used for radial longitudinal dysplasia (Table I) and the Bayne classification system was used for ulnar longitudinal dysplasia (Table II).

Proximal Radial Longitudinal Dysplasia
All patients classified as having proximal radial longitudinal dysplasia demonstrated proximal upper-limb dysplasia characterized by an abnormal glenoid and an absent proximal part of the humerus. These patients all had a recognizable distal part of the humerus, which articulated with the proximal part of the ulna, and radial-sided hand abnormalities.

Proximal Ulnar Longitudinal Dysplasia
All patients classified as having proximal ulnar longitudinal dysplasia demonstrated a hypoplastic glenoid with a single arm/forearm bone that had the proximal characteristics of a humerus and the distal characteristics most similar to a radius. This bone was commonly bifurcated distally. The elbow joint was absent, and there were carpal and hand abnormalities typical of ulnar longitudinal dysplasia. The hand abnormality was typically more severe than that seen with radial longitudinal dysplasia.

Severe Combined Dysplasia
Type A
These patients all had a type-III intercalary transverse deficit (i.e., distal phocomelia) as classified by Frantz and O’Rahilly. Radiographically, they consistently demonstrated a normal-to-hypoplastic shoulder (underdeveloped glenoid), a normal-to-short humerus with a normal distal humeral flare, and absence of both the radius and the ulna. All patients had an abnormal hand. The abnormalities were not confined to one segment of the extremity.

### Materials and Methods
We examined the medical records of all patients with the diagnosis of phocomelia seen between 1960 and 2000 at two dedicated pediatric orthopaedic hospitals, the Texas Scottish Rite Hospital and the St. Louis Shriners Hospital. Institutional review board approval was obtained from both institutions. All patients with a diagnosis of upper-extremity phocomelia who had complete medical records and appropriate radiographs of the upper extremities were included. Additionally, in an attempt to ensure that all patients with a potential diagnosis of phocomelia were identified, radiographs and medical records of patients with a diagnosis of amelia or proximal femoral focal deficiency were also reviewed. Forty-one patients (sixty limbs) with a diagnosis of phocomelia were identified.

All available upper-extremity radiographs for each patient were carefully reviewed, with particular attention paid to three levels. At the proximal level, the scapula, clavicle, glenoid, and proximal part of the humerus were assessed. The distal part of the humerus, the elbow joint, and the forearm were evaluated at the mid-level, and the wrist, hand, and fingers were assessed at the distal level. At each level, the morphology of the affected bone was traced onto plain paper to document the deformities. This allowed comparison among patients and provided an effective method with which to categorize extremities with similar deformities. The medical records and other radiographs, particularly of the spine and lower extremities, were reviewed to determine the presence of associated anomalies.

The tracings were grouped according to the pattern of the deformity: i.e., proximal radial longitudinal dysplasia, proximal ulnar longitudinal dysplasia, or severe combined dysplasia (type A or B).

### Proximal Radial Longitudinal Dysplasia

<table>
<thead>
<tr>
<th>Type</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Short distal part of radius</td>
</tr>
<tr>
<td>II</td>
<td>Radius in miniature</td>
</tr>
<tr>
<td>III</td>
<td>Partial absence of radius</td>
</tr>
<tr>
<td>IV</td>
<td>Complete absence of radius</td>
</tr>
</tbody>
</table>

### Proximal Ulnar Longitudinal Dysplasia

<table>
<thead>
<tr>
<th>Type</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Hypoplastic ulna</td>
</tr>
<tr>
<td>II</td>
<td>Partial absence of ulna</td>
</tr>
<tr>
<td>III</td>
<td>Complete absence of ulna</td>
</tr>
<tr>
<td>IV</td>
<td>Radiohumeral synostosis (extension)</td>
</tr>
</tbody>
</table>
Type B
These patients all had a type-I intercalary transverse dysplasia (i.e., complete phocomelia) as classified by Frantz and O’Rahilly. They consistently demonstrated a complete absence of both the humerus and the forearm segments. All patients had abnormal hand elements attached to an abnormal shoulder.

Evaluation
A comprehensive review of the medical records of each patient was performed. Information concerning maternal risk factors during pregnancy, maternal medical status, difficulties with the pregnancy, birth complications, and family history of genetic disorders was recorded. The medical records were also assessed to identify associated medical problems, syndromic associations, and other musculoskeletal abnormalities.

Results
Proximal Radial Longitudinal Dysplasia
Twenty-nine extremities in sixteen patients (seven female and nine male) were classified as having proximal radial longitudinal dysplasia. The radial longitudinal dysplasia was bilateral in fifteen of the sixteen patients; thirteen patients had bilateral proximal radial longitudinal dysplasia, one had a contralateral type-III radial longitudinal dysplasia as classified by Bayne and Klug, and one had a contralateral type IV radial longitudinal dysplasia. Sixteen extremities had an arc of elbow flexion-extension of >100°, eleven had an arc between 30° and 100°, and two had an arc of <30°.

Twenty-four of the twenty-nine extremities had only an ulna, whereas a portion of the radius was present in four extremities and one limb had a proximal synostosis of a hypoplastic radius and ulna. Distally, nineteen of the extremities had an absent thumb and an array of hand abnormalities: two hands had four fingers, fourteen hands had three fingers, and three hands had two fingers. The other ten extremities (five patients) had a hand with five digits; seven of these extremities were in patients with thrombocytopenia-absent radius syndrome. The most common radiographic appearance was an ulna of relatively normal morphology, with absence of the proximal portion of the humerus and presence of the distal portion (Fig. 1). The size and morphology of the humerus and ulna varied among the patients (Figs. 2-A and 2-B). Some patients were more severely affected, with both a short ulna and a short humerus.

Thirteen patients were born following an uneventful gestation and with an uneventful delivery. The mother of one patient had had preeclampsia that required the use of a diuretic in the third trimester; another patient was born after thirty weeks of gestation and required a prolonged stay in the intensive care unit, and the final patient was born after thirty-six weeks of gestation.

There were multiple associated systemic medical problems. Five patients had congenital heart disease (such as atrial and ventricular septal defects), four had thrombocytopenia-absent radius syndrome, three had congenital kidney disease, and one each had Klippel-Feil syndrome, VACTERL (vertebral, anal, cardiac, tracheoesophageal, renal, limb abnormalities) association, Holt-Oram syndrome, and hypoplastic lung. Another patient had a mild scoliosis, and one patient had a Sprengel deformity. The only additional musculoskeletal abnormality identified was a clubfoot in four patients and knee stiffness in another. One patient had a family history of minor limb abnormalities.

Proximal Ulnar Longitudinal Dysplasia
Twenty extremities in seventeen patients (seven female and ten male) were classified as having proximal ulnar longitudinal dysplasia. The ulnar longitudinal dysplasia was bilateral in five patients; three of them had bilateral proximal ulnar longitudinal dysplasia, one had a contralateral Bayne type-III ulnar longitudinal dysplasia, and one had a contralateral Bayne type-IV ulnar longitudinal dysplasia. Three others had abnormalities in the contralateral extremity: one had a hypoplastic scapula and glenoid and two had type-B severe combined dysplasia. No patient had elbow motion.
Twelve extremities were associated with a shoulder abnormality, commonly hypoplasia of the glenoid. The morphology of the upper-extremity bone resembled a humerus proximally with a distal physis resembling that of a radius. Eleven extremities had a bifurcation of the single bone distally (Fig. 3). Ten extremities had a large medial osseous mass that resembled a medial condyle at the level of what would have been the elbow (Fig. 4).

All extremities had an abnormal hand. Two had a relatively normal thumb with two additional, abnormal digits. Three extremities had a hypoplastic thumb and either two or three abnormal digits. The other fifteen extremities had an absent thumb with an array of hand abnormalities. Syndactyly was common, and motion of the digits was abnormal.

Eleven of the seventeen patients were born after an uneventful gestation and with an uneventful delivery. The
mothers of the other six patients had major intrauterine events. One had gynecological surgery at five weeks of gestation (when it was not known that she was pregnant), one had an unknown illness requiring hospitalization during the first trimester, one had an upper respiratory viral infection in the first trimester and a history of marijuana use during pregnancy, one had toxemia of pregnancy, one used multiple medications (prescription and illegal) in the first trimester, and one had a “significant illness” in the first trimester. One infant was born prematurely at thirty-two weeks, but there were no delivery-related or adverse perinatal events.

Associated musculoskeletal abnormalities were common. Four patients had scoliosis, three had bilateral proximal femoral focal deficiency, three had bilateral fibular hemimelia, one had associated palate abnormalities, and one had Klippel-Feil syndrome. The sibling of one patient had amelia bilaterally.

**Severe Combined Dysplasia**

**Type A**

Seven extremities in seven patients were classified as having type-A severe combined dysplasia. There were four female and three male patients. Four of the seven patients had an abnormality of the contralateral extremity: two patients had a hypoplastic extremity with all segments present, one had amelia, and one had a type-B severe combined dysplasia.

The patients commonly had a relatively normal humeral segment with an essentially absent forearm segment and an abnormal hand (Fig. 5). The shoulder was normal in five patients, and two patients had a hypoplastic glenoid. All seven hands had both thumb and finger abnormalities; one had four fingers and a hypoplastic thumb, two had three fingers and an absent thumb, and four had two fingers and an absent thumb. All patients had shoulder and wrist motion.

One patient was adopted (family history unknown).
One mother had a urinary tract infection treated with antibiotics during pregnancy, and another mother had preeclampsia. Delivery was uneventful for all patients. Three patients had congenital cardiac abnormalities, and two patients had an associated musculoskeletal abnormality: one had proximal femoral focal deficiency and the other, amelia. There was no family history of limb abnormalities.

**Type B**

Four extremities in four patients (two female and two male) were classified as having type-B severe combined dysplasia. All had complete absence of the humerus and forearm segments as well as major hand abnormalities, with either one or two digits (Fig. 6). The contralateral extremity was abnormal in all patients: two contralateral extremities had a proximal ulnar longitudinal dysplasia, one had a Bayne type-II ulnar longitudinal dysplasia, and one had a type-A severe combined dysplasia.

Only one patient was known to have been born after an abnormal gestation: the mother was exposed to a variety of legal and illegal medications during the first trimester. All four deliveries were uneventful. One patient had a congenital cardiac anomaly, one had a cleft palate, one had bilateral proximal femoral focal deficiency, and one had bilateral fibular hemimelia. There was no family history of limb abnormalities.

**Discussion**

Traditionally, major limb deficiencies have been classified as either transverse or longitudinal and as either terminal or intercalary according to a schematic rather than a developmental concept. Genetic and developmental biological research has provided us with a better understanding of early limb development and serves as the basis for an alternative approach to classification.

There are three longitudinal axes of formation: proximodistal, anteroposterior, and dorsoventral. The apical ectodermal ridge controls proximodistal development through fibroblast growth factors. Proximodistal limb arrests are probably caused by abnormalities of the apical ectodermal ridge. The zone of polarizing activity controls the anteroposterior axis, subsequently known as the pre/post axis or the radial/ulnar axis, with progressive fetal development through a morphogen, sonic hedgehog. The apical ectodermal ridge and the
zone of polarizing activity are closely linked by diffusion through a feedback loop.\textsuperscript{13,14,18-21}

While the important roles of the apical ectodermal ridge and the zone of polarizing activity in limb development have become better understood, there remain many unanswered questions concerning the teratologic events leading to limb deficiencies. Ogino and Kato\textsuperscript{16} demonstrated that radial and ulnar longitudinal deficiencies can be induced in rats with administration of Myleran (busulfan). The timing of the Myleran administration determined the type of longitudinal dysplasia: administration at nine to ten days of gestation produced ulnar deficiency, and administration at ten to eleven days of gestation, radial deficiency. The severity of the deficiency was related to the dosage of the Myleran\textsuperscript{15,16}. In another study, exposure of rats to the cytotoxic agent Adriamycin (doxorubicin) at approximately eight days of gestation induced esophageal, tracheal, cardiovascular, vertebral, and limb abnormalities.\textsuperscript{10} Most notably for this discussion, Adriamycin led to limb malformation in 61% of animals with esophageal atresias and involved the humerus in addition to the radius and ulna. Bilateral deficiencies were common.

Our investigation demonstrated that so-called intercalated deficiencies, which are difficult to explain from a developmental biology standpoint, may represent forms of longitudinal deficiencies. The severity of the longitudinal dysplasia is likely related to both the timing and the severity of an insult to the zone of polarizing activity and/or the apical ectodermal ridge.
**Longitudinal Dysplasia**

In 1961, Frantz and O'Rahilly classified phocomelia according to several different patterns of transverse, intercalary segmental dysplasia. In 1976, Swanson summarized the classification adopted by the American Society for Surgery of the Hand and the International Federation of Societies for Surgery of the Hand and questioned the existence of intercalary deformities; the report concluded that “true intercalary deficiencies rarely, if ever, existed” as “all ‘phocomelias’ . . . have some terminal manifestations.” It was suggested that the intercalary deficiencies might be a part of the spectrum of longitudinal deficiencies. Kelikian agreed that true segmental absence was uncommon. Nevertheless, the concept of transverse deficiencies persisted, and the diagnosis of phocomelia has continued to be utilized.

Recently, in 2003, Tytherleigh-Strong and Hooper evaluated the Frantz and O'Rahilly classification of phocomelia and presented their review of the findings in forty-four involved upper extremities. These authors questioned the existence of intercalary defects. The clavicle and scapula were present in all limbs. The lateral aspect of the scapula and the glenoid were always abnormal, and the humeral head, when present, was also abnormal. None of the hands were normal and most were missing at least one digit. Twelve of twenty patients who had abnormalities of both upper extremities had an identical dysplasia bilaterally. Only eleven of the forty-four limbs were classifiable with the Frantz and O’Rahilly system. The other thirty-three limbs had been classified as having phocomelia, but, on review of the findings, Tytherleigh-Strong and Hooper found these limbs to be non-classifiable. They divided these thirty-three into distinct groups. The limbs in Group A had an abnormal humerus with an abnormal single forearm bone; those in Group B had an abnormal humerus, radius, and ulna; and those in Group C had an abnormal humerus fused to a forearm bone or bones. Groups A and C appear to represent the deficiencies that we would classify as proximal radial longitudinal dysplasia and proximal ulnar longitudinal dysplasia, respectively.

Our findings, which were similar to those of Tytherleigh-Strong and Hooper, suggest that phocomelia as a classification term is overused and may be completely incorrect. The deformities in forty-nine of the sixty extremities in our study could be considered a continuum of radial or ulnar longitudinal dysplasia. In those cases, the abnormalities were demonstrated throughout the upper extremity without evidence of an intercalary deficit.

While the deformities in the other eleven extremities were not as clearly classifiable as either a radial or an ulnar longitudinal dysplasia, we think that the term phocomelia is inappropriate for them for three primary reasons. First, all eleven extremities had hand abnormalities in addition to the severe forearm and/or arm dysplasia and none had a true intercalary deficiency. Second, three of the four extremities that were classified as having type-B severe combined dysplasia (formerly known as complete phocomelia) had ulnar longitudinal dysplasia on the contralateral side; this strongly suggests that the deformities in the involved extremities represent severe manifestations in the continuum of ulnar longitudinal dysplasia. Lenz and Feldmann previously noted the relationship between ulnar defects in one extremity and more severe abnormalities (amelia, ulnar defects, humeroradial synostosis, and ectrodactyly) in the other, and they suggested that the association of “such diverse malformations with ulnar defects is suggestive of common etiology”—i.e., bilateral ulnar longitudinal dysplasia. Third, the eleven extremities in our series potentially could be considered as having a combined longitudinal radial and ulnar dysplasia manifested by an absence of both forearm bones (as well as absence of the humerus in type B) with associated hand abnormalities. On the basis of these observations, we propose that upper-extremity disorders previously labeled as phocomelia should be considered to be longitudinal dysplasias.

**Proximal Radial Longitudinal Dysplasia**

The twenty-nine extremities classified as having proximal radial longitudinal dysplasia all had an abnormal shoulder, an absent proximal part of the humerus, an identifiable distal part of the humerus and ulnoumeral joint, a forearm with a normally contoured ulna and an absent or abnormal radius, and an abnormal hand. The hand abnormality resembled that seen in radial longitudinal dysplasia (i.e., an absent thumb and abnormal radial-sided digits), as described by Bayne and Klug.

The classification of these upper-extremity deformities as a severe form of radial longitudinal dysplasia is supported by multiple observations. First, the dysplasia of the elbow, forearm, and hand, if considered alone, would be classifiable as radial longitudinal dysplasia. Second, shoulder dysplasia was previously noted by Bayne and Klug in patients with radial longitudinal dysplasia, although the specific abnormalities were not described. We believe that either these shoulder abnormalities have been ignored when patients have been diagnosed as having radial longitudinal dysplasia (i.e., radial clubhand) or the severity of the proximal dysplasia has led to a diagnosis of phocomelia. Third, the patients whom we diagnosed as having proximal radial longitudinal dysplasia had medical disorders typically seen in association with radial longitudinal dysplasia (such as thrombocytopenia-absent radius syndrome) and infrequently had any other musculoskeletal abnormalities. Fourth, radial longitudinal dysplasia has a high prevalence of bilaterality, and thirteen of the sixteen patients who were classified as having proximal radial longitudinal dysplasia in our study had the abnormality bilaterally. Additionally, in two of the three patients with unilateral proximal radial longitudinal dysplasia, the contralateral extremity demonstrated the findings of radial longitudinal dysplasia described by Bayne and Klug. While it is possible that the patients had two different upper-extremity anomalies, it is more likely that both extremities were affected by the same process.

The standard and accepted classification of radial longitudinal dysplasia does not include a category for the abnormalities in the patients in our series. In 1987, Bayne and Klug provided a classification scheme, consisting of types I through
IV, which was recently supported by James et al.\textsuperscript{11} and expanded to include a type 0. Bayne and Klug based their classification system on the findings in 103 patients, whom they noted had associated proximal upper-extremity anomalies: one patient had a hypoplastic shoulder, one had a humeroulnar synostosis, and one had a proximal phocomelia (not otherwise clarified); however, these abnormalities were not incorporated into the classification system. We think that the extremities in this group represent a severe form of radial longitudinal dysplasia that may be best categorized as a new addition (Type V) to the Bayne and Klug classification (Fig. 7).

**Proximal Ulnar Longitudinal Dysplasia**

The twenty extremities classified as having proximal ulnar longitudinal dysplasia in our study all had a single arm/forearm bone, eleven had a distal bifurcation of that bone, and all had hand abnormalities resembling those seen in ulnar longitudinal dysplasia as reported by Bayne\textsuperscript{7} and by Cole and Manske\textsuperscript{7}. The association between humeral bifurcation and radiohumeral synostosis with ulnar aplasia is well-established\textsuperscript{11,17,24-34}. Humeral bifurcation with humeroradial synostosis and ulnar aplasia with oligodactyly is extremely uncommon (less than one in 50,000 births)\textsuperscript{11}. Previous studies have been limited to case reports found predominantly in the genetics literature\textsuperscript{11,17,26,27,31,34}. While the relationship between radiohumeral synostosis with distal bifurcation and ulnar longitudinal dysplasia has not been specifically noted in the orthopaedic literature, radiographs depicting this constellation of findings can be found in many previous reports on ulnar longitudinal dysplasia\textsuperscript{5,35-37}.

Multiple considerations support the categorization of the disorder in these patients as a severe form of ulnar longitudinal dysplasia. First, radiohumeral synostosis is commonly seen in patients with ulnar longitudinal dysplasia (Table II). Previous authors have recognized that the single, long upper-extremity bone with a distal bifurcation represents a radiohumeral synostosis\textsuperscript{11,17,24-34}. Consequently, the absent ulna and other similarities to the more typical ulnar longitudinal dysplasia strongly suggest that these extremities had a severe, proximal manifestation of ulnar longitudinal dysplasia. Second, two of the seventeen patients had ulnar longitudinal dysplasia as classified by Bayne\textsuperscript{7} on the contralateral side. As noted in the previous discussion concerning proximal radial longitudinal dysplasia, it is possible that these patients had two separate diagnoses, but a common diagnosis is much more likely. Third, associated medical conditions were uncommon and additional musculoskeletal abnormalities were common in this group, findings similar to those noted with ulnar longitudinal dysplasia\textsuperscript{38,39}. Finally, the hand abnormalities seen in our patients were similar to those commonly found in patients with ulnar longitudinal dysplasia\textsuperscript{11,30,38}.

In contrast to the single well-accepted classification of radial longitudinal dysplasia, ulnar longitudinal dysplasia has been classified in a variety of ways, each emphasizing different features\textsuperscript{36,38,40}. While no single classification system has been utilized by all investigators, Bayne’s classification of ulnar longitudinal dysplasia, modeled after the classification of radial longitudinal dysplasia, is used frequently\textsuperscript{7} (Table II). We suggest that a new type (type V) be added to represent cases of severe radiohumeral synostosis with humeral bifurcation or a large medial condyle (Fig. 8).

**Severe Combined Dysplasia**

Although the data are less clear, we believe that the upper-extremity abnormalities that we classified as severe combined dysplasia should also be considered to be longitudinal deficiencies. All seven patients with type-A and all four with type-B severe combined dysplasia had hand abnormalities, thereby challenging the concept of a segmental transverse defect. These deficiencies may represent a combination of both radial and ulnar longitudinal dysplasia or they may simply be a severe manifestation of ulnar longitudinal dysplasia as suggested by the high prevalence of contralateral ulnar longitudinal dysplasia. Additional clinical studies and genetic information are needed to clarify this issue.

**Study Weaknesses**

The primary weakness of our study is that the disorders were classified on the basis of a retrospective review of radiographs and medical records. Furthermore, some radiographs were made when the patients were of a young age, and ossification in the extremities will change the radiographic appearance, potentially altering our classification. Additionally, our patient group may not have been large enough for us to assess the reliability of a new classification system or to modify an existing system. However, we think that, given the rarity of the diagnosis of phocomelia, sixty extremities represent an unusually large group. Finally, our selection of patients for inclusion in this investigation was based on a previous diagnosis of phocomelia. The use of that search criterion may have led to the inadvertent exclusion of some patients with severe proximal limb abnormalities that cannot be classified with the proposed system.  

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