Congenital absence of humerus with preaxial terminal longitudinal hemimelia and hypoplasia of the scapula in a dog: a case report

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ABSTRACT: A case of a unilateral forelimb congenital defect in a three-month-old female puppy dog with clinical and radiographic findings is described here. Congenital absence of humerus with preaxial terminal longitudinal hemimelia is a rare condition in human and animal species. Although similar congenital limb deformities in dogs have previously been documented, the present case is, to the authors’ knowledge, the first report of this type of forelimb hemimelia in a dog, and represents an addition to the scant literature on this topic.

Keywords: aplasia; canine; limb defect; malformations; pathology

As widely reported, birth defects arise from structural or functional congenital malformations stemming from errors during foetal development (Noden and De Lahunta 1985). They can affect an isolated portion of a body system, the complete system or parts of different systems (Dennis and Leipold 1979). Malformations of the extremities or parts of them vary in their manifestations, ranging from absence of a single structure to partial or complete absence of the limbs (Lallo et al. 2001). The term dysostosis is used to define malformations of individual bones or groups of bones, caused by a failure of bone model formation or failure of the transformation of the bone model into cartilage or bone (Noden and De Lahunta 1985; Towle and Breur 2004).

Embryologically, the aggregation of the somatic mesoderm cells of the hypomere beneath the surface ectoderm to form the limb bud is known to be the primary step in limb formation (Noden and De Lahunta 1985). Vertebrate limb buds are embryonic structures for which many of the molecular and cellular mechanisms that control pattern formation during development are known. Specialised regions of the developing limb bud, such as the zone of polarising activity (ZPA), the apical ectodermal ridge (AER), and the non-AER ectoderm, direct and coordinate the development of the limb bud along the three axes, giving rise to a stereotypical pattern of elements well conserved among tetrapods. Specific gene functions have been shown to mediate the organising and patterning activities of the ZPA, the AER, and the non-AER ectoderm (Capdevila and Izpisua Belmonte 2001). The AER is a specialised epithelium located at the distal edge of the limb bud (Casanova et al. 2011). The Fibroblast growth factor (FGF) secreted by the mesenchyme cells to induce the AER is probably FGF10 (Xu et al. 1998; Yonei-Tamura et al. 1999). Other FGFs, such as FGF2, FGF4, and FGF8, will also induce an AER to form; but FGF10 appears to be the FGF synthesised at the appropriate time and in the appropriate places (Gilbert 2000). The zone of polarising activity (ZPA) is a group of mesenchymal cells located in the posterior region of the limb bud; the Sonic hedgehog (Shh) gene mediates the polarising activity of the ZPA (Riddle et al. 1993). Finally, expression of the Wnt7a gene from the dorsal non-AER ectoderm of the limb bud and engrailed-1 (EN-1) from the ventral aspect are involved in specifying the dorsal-ventral axis (Keith et al. 2013).
The aim of this report is to describe the macroscopic and radiographic findings of a unilateral forelimb defect observed in a dog.

**Case description**

A three-month-old female cross-breed puppy dog was evaluated for an obvious deformity in its left forelimb. Its prior history was unknown as it was an orphan; the observed deformity of the forelimb was congenital. This deformity had caused limited mobility since its birth, because the dog held the paw in flexion.

The site of deformation was assessed by physical and radiographic examination.

Forelimb radiographs were prepared using an Analogic Radiographic/Fluoroscopic Table System (Dedalus Mb 90/20 IMX-2A, Imago Radiology S.r.l., Abbiatigrasso (MI), 20081, Italy) with a digital radiography system (Fujifilm Medical Systems, Italy) in different projections: mediolateral and oblique views, X-ray settings of 55 kV, 10 mAs at a film focus distance of 100 cm, without grid, were the settings used.

At physical examination, a non-functional left forelimb, markedly reduced in size, with varus deformation of the forepaw was seen. The paw was characterised by the presence of only three digits (Figure 1).

The radiographs showed hypoplasia of the scapula, total aplasia of the humerus, radius and complete aplasia of two digits (phalanges and metacarpal bones of digit 1 and digit 2).

The anconeal and coronoid processes of the ulna were malformed and appeared very close to each other; the trochlear notch was clearly reduced; 90° varus deviation with rotation of the ulnocarpal joint was also observed. Only ulnar, radial and accessory carpal bones were present (Figure 2). No surgical treatment was performed.

**DISCUSSION AND CONCLUSIONS**

The survey radiographs revealed the absence of humerus, radius, carpal bones and phalangeal bones with hypoplasia of the scapula. The description of limb malformations is often complicated by the lack of a uniform and precise nomenclature.

The case here described was named with the term hemimelia; this term indicates a congenital abnormality characterised by complete or partial absence of one or more bones (Towle and Breur 2004); the absence of a part of a limb (e.g. carpus) is termed ectromelia (ectro = absence of a part) (Noden and De Lahunta 1985).

The term ‘ectromelia’ was coined by Isidore Geoffroy Saint-Hilaire in the early 19th century. He introduced the term in analogy with ‘ectrodactylyia’, in which the prefix ‘ectro-’ is derived from the Ancient Greek verb ἔκτρωειν (ektrooein): ‘carrying out an abortion’ (hence ‘deliberately taking outside’). Ectromelic limbs are classified on the basis of the affected limb segment. For example, ectromelia of the stylopodium refers to a limb that terminates anywhere along the femur or humerus, ectromelia of the zeugopodium denotes termination along the radius and ulna or tibia and fibula, and ectromelia of the autopodium describes termination at the bones of the manus. At first, the term “ectromelia” was used only for a complete or almost complete absence of one or more limbs. However, the term was more recently superseded...
by the official term “amelia”, not commonly used at that time, although it is now listed in the official Nomina Embryologica Veterinaria. As amelia means the ‘absence of a limb’, such a term cannot be used for limbs missing some major parts, but still containing some other limb fragments; hence, ectromelia is used for this condition. However, the term ‘ectromelia’ does not specify what parts are missing and what parts are present, whilst the hemimelia as specified by Towle and Bruer (2004) is a precise description of what is wrong with the limb.

Thus, hemimelia is a congenital abnormality characterised by the complete or partial absence of one or more bones (Towle and Bruer 2004); hemimelia is intercalary when all or part of the middle bones of a limb are absent, with the proximal and distal portions being present. On the other hand, longitudinal hemimelia indicates the absence of one or more bones along the preaxial (medial) or postaxial (lateral) side of the limb (Mo and Manske 2004; Towle and Breur 2004). Hemimelia results from a lack of AER-mesodermal interaction during limb outgrowth (Rantanen and Hegreberg 1982; Towle and Breur 2004).

Other terms describing limb malformations include phocomelia, a congenital abnormality characterised by the absence of a proximal portion of a limb (Dennis et al. 2001); brachymelia, which indicates hypoplasia and aplasia of the distal limb segments (Cornillie et al. 2004); aphalangia, which describes the absence of one or more phalanges from one to four digits (Macrì et al. 2012); adactyly, which is commonly used when referring to the peculiarity of the total absence of digits (Noden and De Lahunta 1985).

These different forms of hemimelia/ectromelia have been reported in domestic animals: brachymelia (Cornillie et al. 2004), hemimelia in dogs (Pedersen 1968; Alonso et al. 1982; Schultz and Watson 1995; Ahalt and Bilbrey 1997; Lallo et al. 2001; Rahal et al. 2005; Alam et al. 2006), hemimelia in cats (Pisoni et al. 2012), ectromelia in cat (De Lima 1915; Macrì et al. 2009), adactyly (Barrand and Cornillie 2008; Macrì et al. 2011), aphalangia (Macrì et al. 2012), radial agenesis in dogs and cats (Swalley and Swalley 1978; Richardson 1979; Betts 1981; Winterbotham et al. 1985; O’Brien et al. 2002; Gemmill et al. 2004; Rahal et al. 2005; Hildreth and Johnson 2007; McKee and Reynolds 2007).

Possible causes of hemimelia include administration of chemotherapeutics (tetracycline, gri-seofulvin, parabendazole, etc.), malnutrition (lack of riboflavin), drug intake such as thalidomide or corticosteroids (in chick embryos), transplacental virus infections and x-rays, dietary mineral deficiency (e.g., zinc, manganese, copper) and vaccines (Johnson 1965; Karnofsky 1965; Warkany 1965; Riddle and Leighton 1970). Other causes of distal limb absence in young animals include strangulation by restrictive bands, in utero accidents and postnatal traumas (Johnson et al. 1995).

Abnormalities in the function of the molecules responsible for embryonic limb development along the three main axes are responsible for embryo limb developmental malformations. Especially in the human, chick and mouse embryo mutation of Wnt7a, En-1, FGF-2, Shh and Lmx-1 genes have been linked to development of hemimelia (Chiang et al. 2001; Towle and Breur 2004; Woods et al. 2006). Also, hemimelia results from a lack of AER-mesodermal interaction during limb outgrowth (Ogden and Grogan 1987).

The critical period for the development of the entire limb in the canine embryo is between the
3rd and 4th weeks of gestation, when tissues are more susceptible to external influences (Noden and De Lahunta 1985).

The heritability of radial hemimelia has been suggested. Alonso et al. (1982) described an autosomal recessive form of hemimelia in Chihuahuas; Hoskins (1995) suggested that hemimelia in Siamese and domestic shorthair cats may be a hereditary trait.

Since we were unable to study littermates or the parents of the affected dog, nor the environmental circumstances of the bitch, the cause of the condition in this case remains unclear. Although congenital limb deformities in dogs have previously been documented, the congenital absence of humerus with hypoplasia of the scapula represents an extreme variant of hemimelia. Indeed, the present case is, to the authors’ knowledge, the first report of this type of forelimb malformation in a dog, and represents an important addition to the literature on this topic.

REFERENCES


Macri F, De Majo M, Rapisarda G, Mazzullo G (2009): Two cases of feline ektromelia: autopodium ectrome-


Richardson DC (1979): Radial agenesis. Journal of Veterinary Orthopaedics 1, 39–42.


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