Early Onset Cervical Spine Abnormalities in Loeys-Dietz Syndrome

Sara K. Fuhrhop, BS
Mark J. McElroy, MS
Harry C. Dietz, MD
Paul D. Sponseller, MD

JOHNS HOPKINS
MEDICINE

Background

- Loeys-Dietz Syndrome (LDS) is an autosomal dominant connective tissue disorder caused by mutations in the TGF-βR1 and TGF-βR2 genes.
- LDS is characterized by vascular tortuosity and aggressive aneurysms formation, craniofacial abnormalities, and musculoskeletal abnormalities.
- Although vascular abnormalities are the primary cause of morbidity and mortality, recognition of the musculoskeletal features of LDS may facilitate earlier diagnosis and treatment.
- Cervical spine defects or instability have been reported in 19% of patients with LDS, however, these findings were identified among a sample of patients of all ages.

JOHNS HOPKINS MEDICINE

Objectives

This study aims to quantify the prevalence of cervical spine abnormalities in LDS patients ≤ 10 years old.

JOHNS HOPKINS MEDICINE

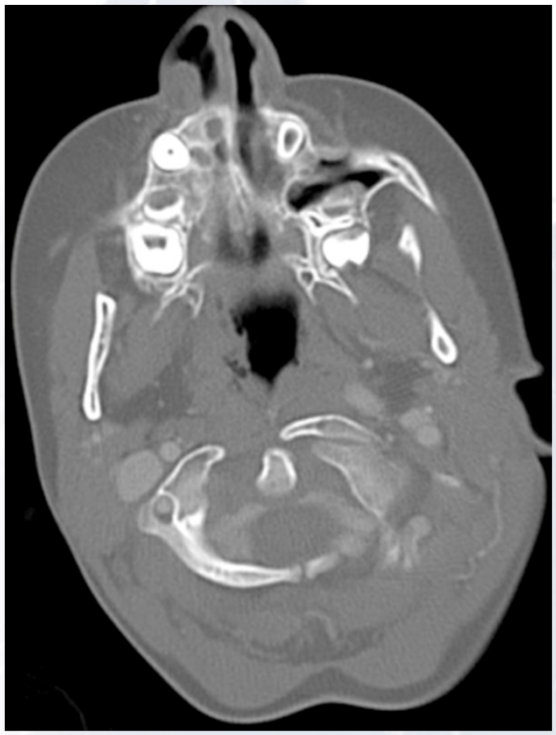
Methods

- IRB approval
- Patient population
  - 42 patients diagnosed with LDS
  - 64% female, 36% male
  - Age ≤ 10 years (median 6.8 ± 3.5, range 1.3-10.5) at time of imaging
  - Average length of follow up 5.3 years
- Data collection
  - Retrospective review
  - Cervical spine neutral, flexion, and extension x-rays
  - Cervical spine computed tomography
  - Some imaging modalities were not available for all patients, so results are reported as a fraction of those imaged.

JOHNS HOPKINS MEDICINE

Results
Vertebral Anomalies

Anomaly	Number of Patients	Percentage of Patients
Anterior Arch Defects C1	10	30.3%
Posterior Arch Defects C1	7	21.2%
Vertebral Hypoplasia C2-C7	4	12.1%
Elongated Odontoid Process	9	26.5%
Posterior Odontoid Angulation	5	14.7%
Off-center Odontoid	15	42.8%

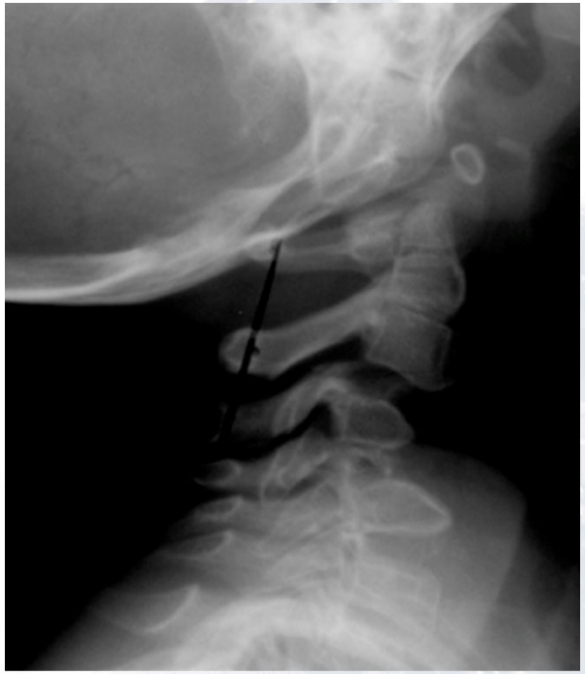


6-year-old female with anterior and posterior arch defects at C1

JOHNS HOPKINS MEDICINE

Results
Kyphosis and Scoliosis

- Cervical scoliosis > 15˚
  - 5 of 33 patients (15.2%)
  - Cobb magnitude 21.2 ± 13.3˚
- Focal kyphosis
  - 13 of 31 patients (41.9%)
  - Cobb magnitude 22.1 ± 23.7



2-year-old female with hypoplastic vertebrae and 24˚ C3-C5 focal kyphosis

JOHNS HOPKINS MEDICINE

Results
Cervical Spine Instability

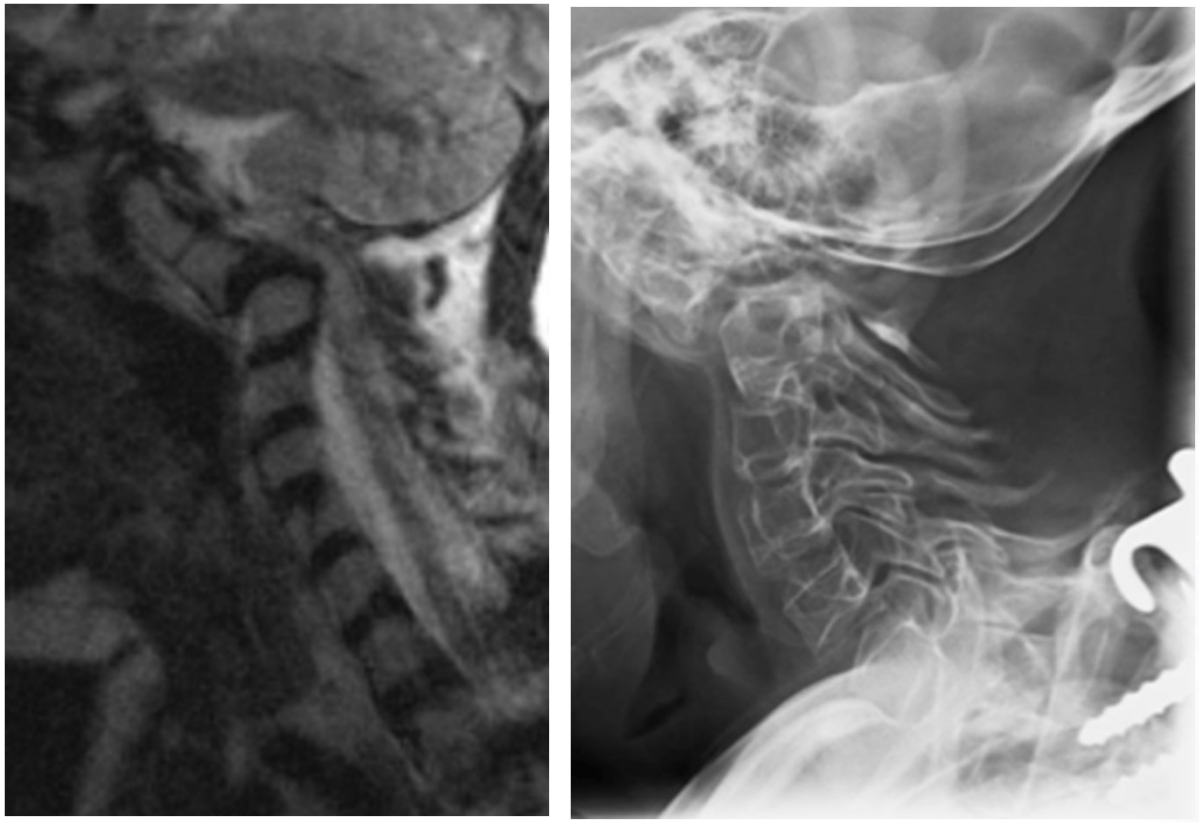
- Cervical spine instability in 18 of 40 patients (45%)
  - Mean age at diagnosis of instability 5.9 years, range 1.0 – 10.75 years
  - Atlanto-axial instability in 5 of 40 patients (12.5%)

    Subluxation of C1-C2 > 3.5 mm in neutral position or subluxation of C1-C2 > 3.5 mm from the neutral position on flexion/extension
  - C2-C7 instability in 14 of 40 patients (35.0%)

    Subluxation of C2-C7 > 3.5 mm in neutral position or subluxation of C2-C7 > 3.5 mm from the neutral position on flexion/extension
- Treatment
  - 7 patients required surgical fusion for cervical spine instability
  - Mean age at surgery 5.3 years, range 1.25 – 10.75 years
  - Postoperative complications
    - Implant loosening with pseudoarthrosis in one patient
    - Pseudoarthrosis without implant loosening in two patients
    - 7 reoperations for complications

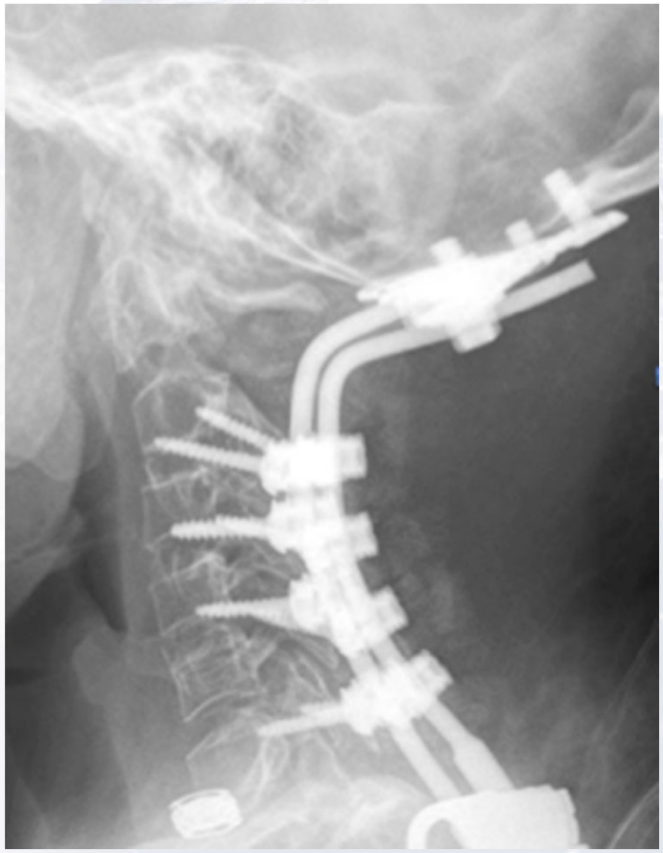
JOHNS HOPKINS MEDICINE

Results
Cervical Spine Instability



Preoperative MRI and radiograph of a 10 year old girl with cord compromise secondary to C2-C3 kyphosis and subluxation

Postoperative radiograph following occiput to T3 posterior fusion, suboccipital craniectomy, and C1-C2 laminectomies



Results
Other Neuraxis Abnormalities

- Chiari I malformation
  - 6 of 36 patients (16.7%)
  - 2 patients required surgical decompression
- Craniosynostosis
  - 5 of 42 patients (11.9%)
  - 2 patients required cranial vault reconstruction

JOHNS HOPKINS MEDICINE

Limitations

1. Age: Some patients have not reached age 10.

1. Records: We do not have a complete set of radiographic data for all patients.

1. Sampling bias: The more severely involved patients may have been treated at our institution.

Conclusions

- Craniocervical midline defects, deformity, instability, and neuraxis abnormalities are common in children with LDS.
- Cervical spine deformity may require periodic re-screening of the cervical spine in children with LDS.
- The prevalence of cervical spine abnormalities in this age group may be greater than previously reported in LDS patients of all ages.

JOHNS HOPKINS MEDICINE

References

1. Erkula G, Sponseller PD, Paulsen LC, Oswald GL, Loeys BL, Dietz HD. Musculoskeletal findings of Loeys-Dietz Syndrome. J Bone Joint Surg Am. 2010;92:1876-1883.
2. Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, Meyers J, Leitch CC, Katsanis N, Sharifi N, Xu FL, Myers LA, Spevak PJ, Cameron DE, De Backer J, Hellemans J, Chen Y, Davis EC, Webb CL, Kress W, Coucke P, Rifkin DB, De Paepe AM, Dietz HC. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet. 2005;37:275-81.
3. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, De Backer JF, Oswald GL, Symoens S, Manouvrier S, Roberts AE, Faravelli F, Greco MA, Pyeritz RE, Milewicz DM, Coucke PJ, Cameron DE, Braverman AC, Byers PH, De Paepe AM, Dietz HC. Aneurysm syndromes caused by mutations in the TGF-beta receptor. N Engl J Med. 2006;355:788-98.
4. Elster AD, Chen MY. Chiari I malformations: clinical and radiologic reappraisal. Radiology 1992; 183:347-353.
5. Kim CW, Perry A, Garfin SR. Spinal instability: the orthopedic approach. Semin Musculoskelet Radiol 2005; 9:77-87.
6. Rojas CA, Bertozzi JC, Martinez CR, Whitlow J. Reassessment of the craniocervical junction: normal values on CT. AJNR Am J Neuroradiol 2007; 28:1819-1823.

JOHNS HOPKINS MEDICINE