

A fracture, a family, legal entanglement, expensive investigation, and a familiar disease

Ujuchukwu Okpechi¹

Kevin Regis²

Rosibell Arcia¹

Kenneth Soyemi^{1,2}

¹Department of Pediatrics,

²Department of Emergency Medicine, Cook County Health and Hospitals System, John H Stroger Jr Hospital, Chicago, IL, USA

Abstract: Osteogenesis imperfecta can be commonly mistaken for child abuse because of similar pattern of injuries. AA is a 3-week-old baby who presented to our emergency department with excessive crying. Skeletal survey revealed subacute spiral fracture of the right humerus, right posterior eighth and ninth ribs, acute fracture of the left femur, bowing of tibia and femur, and osteopenia. Subsequent geneticist examination and genetic testing noted blue sclera and heterozygosity for a variant of *COL1A* gene.

Keywords: fracture, legal, investigation, infant

Introduction

Osteogenesis imperfecta (OI) can be commonly mistaken for child abuse because of similar pattern of injuries. Most cases are autosomal dominant mutations of type 1 collagen genes.¹⁻⁴ It is important to acknowledge physical finding and order genetic testing early to prevent hardship to families and decrease medical expenditure.

Patient and observation

AA is a 3-week-old baby who presented to our emergency department (ED) with excessive crying. Parents noticed decreased movement of the left leg and right arm preceding the onset of AA's sudden irritability. Parents denied recent fall, direct trauma, or shaking AA who lived with parents and two older siblings in a rented apartment in the city while visiting from Africa. There was no family history of easy bruising or fractures, domestic violence, drug/alcohol use, or involvement in social services. ED examination showed growth parameters at 10th percentile; AA was irritable and inconsolable with limited contralateral extremity movement; no bruising, pattern marks, or oral injuries were identified. Skeletal survey revealed subacute spiral fracture of the right humerus, right posterior eighth and ninth ribs, acute fracture of the left femur (Figure 1), bowing of tibia and femur, and osteopenia. Computed tomography scan was normal. MRI/MRA brain revealed left subacute subdural hemorrhage and right parieto-occipital calvarial flattening. Vital signs were normal, other screening laboratory tests were normal; eye examination was negative retinal hemorrhage. Department of Children and Family Services (DCFS) was notified for concern of nonaccidental trauma (NAT); siblings were taken into temporary DCFS custody. Subsequent geneticist examination and genetic testing noted blue sclera and heterozygosity for a variant of *COL1A* gene. Genes evaluated included *BMP1*, *COL1A1*, *COL1A2*, *CRTAP*, *FKBP10*, *IFITM5*, *P3H(LEPRE1)*, *PLOD2*,

Correspondence: Kenneth Soyemi
Departments of Pediatrics and Emergency Medicine, Cook County Health and Hospitals System, John H Stroger Jr Hospital, 1901 West Harrison Street, Chicago, IL 60612, USA
Tel +1 708 300 4350
Fax +1 800 746 3609
Email ksoyemi@cookcountyhhs.org

PLS3, *PP1B*, *SERPINF1*, *SERPINH1*, *SP7*, *TMEM38B*, and *WNT1* (Figure 2). Result was positive for COL1A coding DNA: C.371 G>T variant: pGly224Val (G224V) zygosity: heterozygous classification: pathogenic variant; no other reportable variants were detected by sequencing of the genes included on this panel. A written informed consent has been provided by the patient's parents to have the case details and any accompanying images published for this study.

Discussion

As visitors to USA, parents were unfamiliar with DCFS operations; subtle cultural differences may have led to communication barrier as parents needed time to process the sequence of events cascading from the diagnosis of fractures and NAT. This was confounded by the emotional stress and uncertainty about safety of their children who were taken into custody with strangers. After AA's diagnosis was confirmed, parents reappeared in front of a judge who cleared AA for discharge and travel to country of parent's origin for continuation of care. AA is heterozygous for the G224V pathogenic variant in the *COL1A1* gene, consistent with a molecular diagnosis of autosomal dominant OI. Targeted array comparative genomic hybridization analysis with exon-level resolution of the genes on this panel yielded uninterpretable results due to suboptimal quality of the DNA obtained from the submitted specimen. Most

pathogenic variants in *COL1A1* are sporadic.^{5,6} Because of the potential for mosaicism in an unaffected parent, variant-specific testing of the parents of AA was made available to help determine if the variant was inherited or arose de novo; in addition, this will provide information required for accurate genetic counseling for this family. Parents did not complete testing as of time of writing; if neither parent is found to carry the G224V variant in the *COL1A1* gene, the possibility of mosaicism cannot be excluded, and offspring of either parent may be at risk of carrying this variant. Molecular prenatal diagnosis is available in future pregnancies, if desired; genetic counseling is recommended to discuss the implications of this test report. This multifaceted clinical investigation involved the use of resources; for analysis, cost was stratified into four categories: 1) hospital, 2) social, 3) legal, and 4) family. For hospital services, intensity of service included nine inpatient admission days, 14 specialty consultations (with five services), 23 laboratories, and seven radiological encounters. Laboratory panel testing and services accounted for 47% of AA's encounters (Figure 3). Social worker, legal services including family court appearances, and DCFS investigative services all contributed to the overall cost. The estimated cost of investigating AA's fractures using medical consumer price index easily surpassed \$500,000 when all the cost factors and drivers are considered.⁷

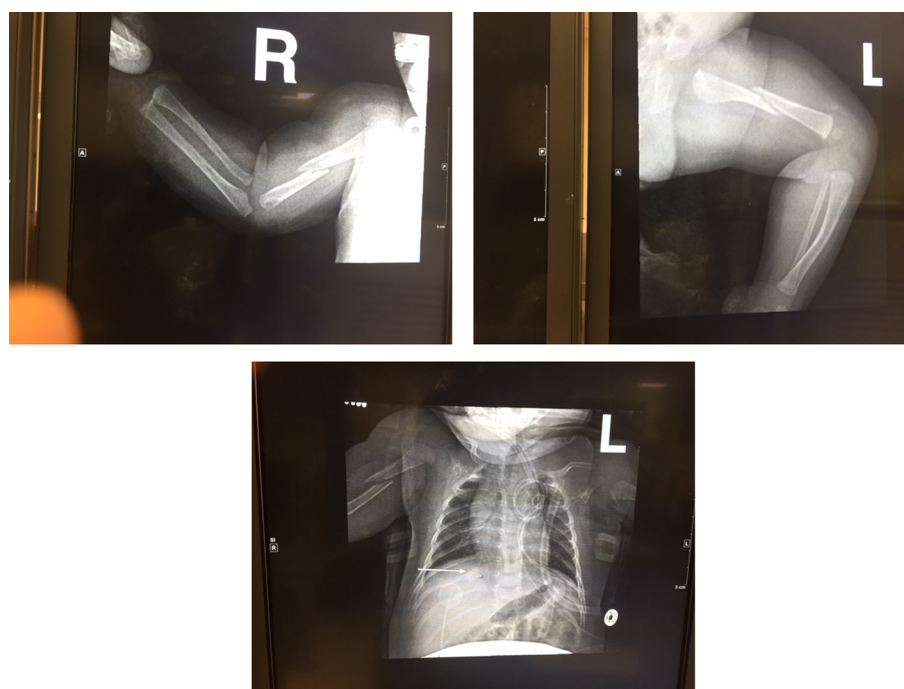


Figure 1 Fractures at initial presentation.

Abbreviations: R, right; L, left.

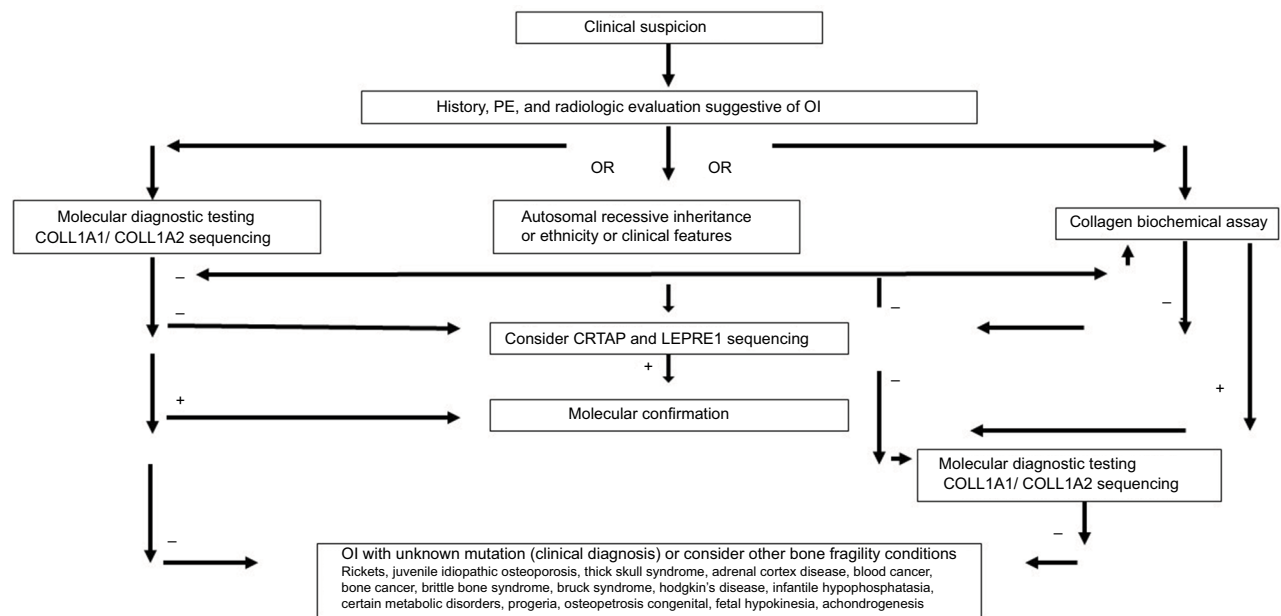


Figure 2 Algorithm for evaluation of osteogenesis imperfecta.

Abbreviations: OI, osteogenesis imperfecta; PE, physical examination.

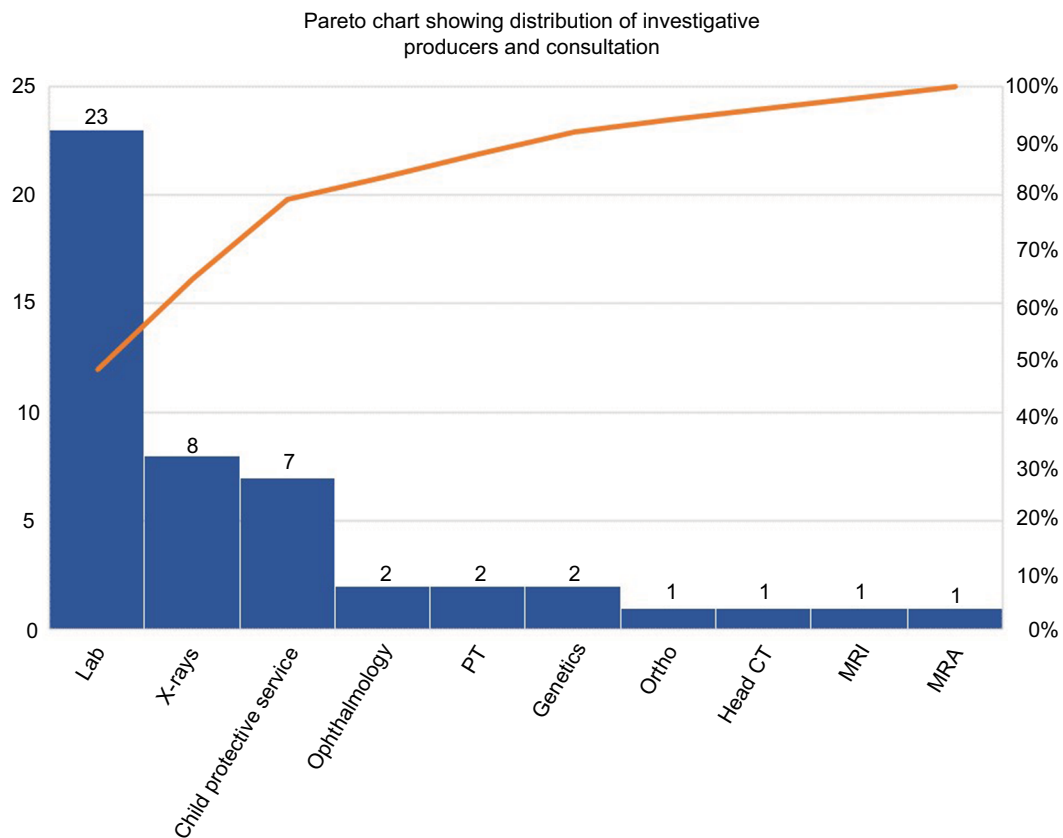


Figure 3 Services and consultation.

Abbreviations: CT, computed tomography; PT, physical therapy.

Conclusion

It is important in the initial investigative phases of unexplained fractures, families should be promptly provided social and psychological resources to help them cope with the unfortunate circumstances.⁸ The extent of such investigations when signs suggestive of confounding systemic diseases and consistent history should be balanced to ensure child safety as well as limit unnecessary expenditure.

Disclosure

The authors report no conflicts of interest in this work.

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