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Osteogenesis Imperfecta: Clinical Features and Management in a Developing Country

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Summary

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Background: Osteogenesis imperfecta (OI) is a rare congenital disorder leading to increased bone fragility.

Objective: To describe the clinical spectrum of OI and report the Ivorian experience in managing this condition.

Settings: Yopougon and Treichville Teaching Hospitals and "Don Orione" Centre for the Crippled in Côte d'Ivoire.

Subjects and Methods: Fifteen OI patients (ten boys and five girls) aged seven days-six years (mean, 2.1 years) from 14 separate families were reviewed for demographics, genetic and clinical patterns, treatment required and outcome. Theywere classified using the criteria of Sillence with comparison to those of Maroteaux and treated depending on OI severity status, by oral preventive drugs, conservative and/or surgical means. All were assessed for fracture rate, functional abilities and ambulation levels.

Results: According to Sillence2 s classification, there were 8 type III, 2 type II and IV, 2 type I and 1 unclassified type which distribution following the criteria of Maroteaux showed 12 (80 percent) prenatal forms (8 severe, 2 regressive and 2 lethal) and 3 (20 percent) postnatal forms (2 generalized and 1 localized). Autosomal dominant inheritance was presumed in two sibs versus 13 private neomutations. In the prenatal group, two-thirds of cases sustained e"20 fractures requiring surgical management on eight occasions versus less than 10 fractures managed closely in other types. At a mean follow up of 5.3 years, one type II patient died perinatally but the other survived with major disabilities. Six type III patients had severe altered functions in which two were chair-bound, one type IV had a restricted ambulation level, and all type I cases had good outcome, while the rest were lost to follow up.

Conclusion: The clinical presentation of osteogenesis imperfecta appears to be classical in these Ivorian children.

Key words: Osteogenesis imperfecta, child, Ivorian, genetic disease, treatment.

Introduction

OSTEOGENESIS Imperfecta (OI) which is one the most important osteochodrodysplasia, depicts a group of skeletal disorders with fragile bones due to anomalies of type I collagen.[1] In the past, a mild form with infrequent fractures called Lobstein2 s[2] disease was described in addition to the severe one which, with multiple fractures is associated with perinatal mortality named Porak & Durante2 s[3] disease. Currently, there is a wide variety of clinical expressions classified by Sillence[4] into four types that have the most widespread usage and into four prenatal and three postnatal forms according to Maroteaux.[5] The treatment of OI is principally palliative by either closed or surgical means due to a lack of an effective therapy. Recent biphosphonates therapies that improve the bone mineral density offer new therapeutic approaches. In this communication,

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we describe the clinical presentation and management of OI in the Ivorian child in our Institutions.

Subjects and Methods

The charts of 15 OI patients from 14 separate families, seen at Yopougon and Treichville Teaching Hospitals (Abidjan) and 2 2 Don Orione2 2 Centre for the Crippled (Bonoua), from January 1992 - December 2004, were reviewed for age and gender, inheritance, clinical patterns, treatment required and outcome. The classification of their clinical entities was based on Sillence's criteria (*type I benign*: mild bone fragility, blue sclerae; *type II lethal*: severe with fractures, perinatal death; *type III grave*: mild fracturing and bowing; *type IV mild*: less severe than type III; autosomic dominant and recessive inheritances for types I-IV and types II-III, respectively) with comparison to those of Maroteaux that defined three prenatal forms (lethal, severe and regressive; private neomutation) as those with in utero and birth fractures, and four postnatal forms (moderate, generalized, localized and those with hyperplastic callus; autosomic dominant or private neo mutation patterns) which present with fractures usually after the walking age. The treatment of our cases consisted in preventive oral therapies followed if necessary, by closed or surgical means for fractures and bowing. Oral therapy consisted of vitamin D of at least 800 IU per day with calcium of at least, 1g per day. Closed treatment by either splinting or casting was relied on for short periods ($\leq$15-21 days) while pinning and nailing were used for internal fixation. The clinical assessment was based on fracture rates, functional abilities and ambulation levels at an average follow up period of 5.3 years.

Results

The point prevalence of osteogenesis imperfecta at birth was estimated at 1 per 45 000 live births during the study period. Seven of the children were neonates, three were aged one month - three years and the rest > three years at the time of diagnosis (mean, 2.1 years). Summaries of their clinical patterns according to both classifications are shown in Table I. Prenatal forms prevailed, accounting for 12 (80 percent) of the 15 cases. In this group, no family history was found in either ancestors or siblings and type III (54 percent) was the most prevalent clinical presentation followed by types II and IV. Their evolution showed the following: one type II died perinatally of pulmonary distress while the other survived but was lost to follow up around the walking age; two-thirds of them sustained at the least 20 fractures with an overall fracture rate of 12.6 per year, while kyphoscoliosis with dwarfism occurred in half of the cases. All were initially managed closely but significant skeletal bowing later required surgical procedures using nailing in four cases, pinning in three and both in one. Six children with type III disease had serious altered functions resulting in their being chair-bound in two (25 percent) and limited ambulation level (75 percent). One of the six required orthesis for walking due to substantial leg-length discrepancy and another had experienced a hyperplastic callus formation. One patient with type IV had restricted ambulation level. The remaining three patients including two type III and one type I, for whom sitting balance was not achieved at three years of age, were lost to follow-up. In the postnatal group, two of three type I children were sibs and had a positive family history that suggested an autosomic dominant pattern of inheritance. We observed a low rate of fractures numbering less than 10, which were all treated by splinting or casting and the presence of blue sclerae in one case. A satisfactory outcome was achieved in this group of patients. None of the patients in this series has so far, developed abnormalities of dentinogenesis.

Discussion

Epidemiology

The prevalence of OI is variously rated in the literature

Table I

Clinical Spectrum of Osteogenesis Imperfecta according to Maroteaux and Sillence's Criteria

	Maroteaux	*Sillence*	*No. of Patients*	*Percentage*	
Prenatal forms	Lethal (L)	Type II	2	13	
	Severe (S)	Type III	8	54	12 (80%)
	Regressive (R)	Type IV	2	13	
	Moderate	-	-		
Postnatal forms	Generalized	Type I	2	13	
	Localized	-	1	7	3 (20%)
	With hyperplastic callus	-	-		
Total			15	100	

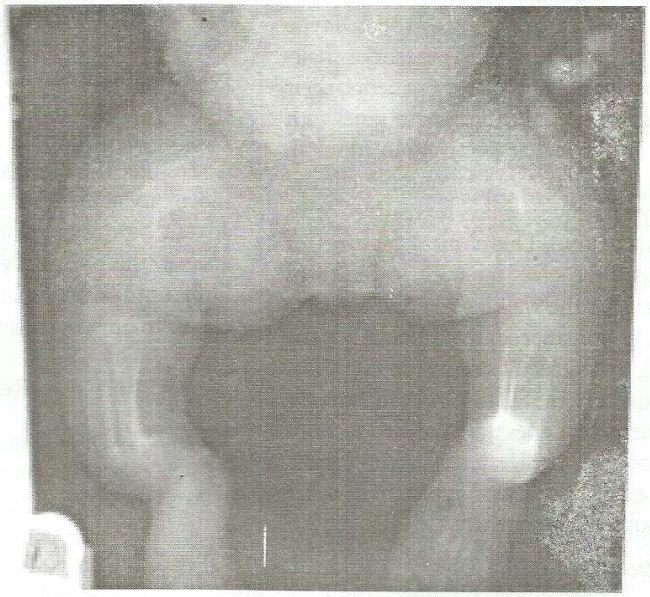

Fig. 1: X-ray of the lower limbs showing excessive bone transparency with shortened and bowed extremities in a newborn infant. Faint callus of the long bones suggested healing fractures. A diagnosis of osteogenesis imperfecta was established by the occurrence of additional fractures.

principally due to its great heterogeneity, but our findings are similar to the main reported rates of 1 per 25 000 to 50 000 live births.[6] By contrast, Karray[7] and Nko'o[8] have reported a higher rate than ours in Tunisia and Cameroon, respectively. However, care must be taken in interpreting African rates which may not represent the true incidence compared with those obtained from population-based studies in the more developed countries. Besides, our series did not take into account the frequent out-of-hospitals births in our rural inhabitants. In addition, the late diagnosis in our patients contrasts with the recent practice of prenatal diagnosis in the more advanced countries. The predilection for the female child seen in our series has also been reported by previous workers but there has so far, been no satisfactory explanation for this.[6-8]

Genetics

Current genetic data suggest private mutation with low recurrence risk for the prenatal forms in opposition to Sillence's[4] earlier statements. The absence of a positive family history in our series supports this inheritance mode even if the possibility of a parental mosaicism could not be ruled out since karyotype studies were unavailable for these patients at the time of this review.[9] Postnatal forms are thought to be governed by an autosomic dominant inheritance with recurrence risk in half of the cases.[4] The involvement of two of our three patients with this form, who were sibs from the same affected mother but different healthy fathers, was suggestive of this mode of inheritance.

Clinical spectrum

As in Maroteaux[5] series, we noted primacy of prenatal forms where severe forms prevailed with respectively of 58 and 66 percent of cases. Conversely, Sillence et al.[4] reported a high rate (87.3 percent) of OI type III for which they predict a constant perinatal death; but their incidence might be overrated since along with Maroteaux[4] some have proved to be compatible with survival. Agreeing with this author, one of ours with typically numerous fractures and major skeletal bowing at birth has survived unlike Sillence2 s[4] beliefs. Currently, the singular "bamboo ribs" radiologic aspect depicted by countless rib fractures is considered as a reliable indicator of lethal form, but some with thin and unfractured ribs as in our survivor have also been reported reflecting the need for a better delineation of these forms.[10,11] The poor prognosis in survivors is illustrated in our case who had developed major scoliosis and failed to gain sitting balance at walking age at the last follow up. Regarding OI type III (S), they presented typically with fractured, shortened and bowed limbs and growth retardation with scoliosis and an ensuing mild to severe dwarfism. In one of them, the severity of growth disturbances affecting one limb with the resulting substantial leg-length discrepancy adds force to the hypothesis c

localized forms described by Maroteaux.[5] By the same token, this author mentioned the exceptional nature of hyperplastic callus formation noted in one OI type III patient.[5] On the whole, with 25 percent of chair-bound and 75 percent of ambulatory patients, their evolution was less severe than in Shapiro's[12] series with rates of 59 and 33 percent, respectively. In addition, two of them who had a more favourable clinical course probably had the so-called regressive forms defined by Maroteaux.[5] The clinical features of postnatal forms were classical with low rate of fractures occurring at the walking age, but the blue sclerae formerly considered by Sillence as the hallmark of OI, and defective dentition were not constant. Subsequently, the Sillence's classification is open to criticism since it does not take into account the overall view of the clinical features. In our opinion, the criteria defined by Maroteaux[4] appear to be more apt to the undoubted heterogeneity of OI.

Treatment options

From a practical viewpoint, the patients can be divided into two groups: those with the mild form who had infrequent fractures and good response to closed treatment and another group of patients with severe forms who sustained severe fractures and bowing of the limbs which required surgical management. Like the experience of other workers, we encountered difficulties in controlling fractures in very young patients and often, little residual deformities must be accepted. Furthermore, most workers advocate the limitation whenever possible, of the period of immobilisation to minimize disuse osteoporosis. The current surgical trend indicated in severe forms after the ages of two or three years consists of a preventive closed intramedullary extensible nailing of weight-bearing limbs followed by intensive physical care and walking programme.[13] Such ideal timing could not be planned in our patients because of limited economic and technical resources. Likewise, we could not prevent the occurrence of dwarfism in our patients since we as yet do not have the knowledge of techniques of spinal arthrodesis.[14] Thus, our experience are confined to the surgical management of cases of re-fracturing with limb bowing using nails or pins either by open or closed means. The medical treatment of OI, based in our practice on vitamin and calcium administration, has long been largely ineffective in altering the course of the disease. Recent studies conclude that intravenous or oral biphosphonates are effective in increasing bone mineral density with the result of fracture rate reduction.[15] Due to their exorbitant costs, these are yet still out of reach for our population.

Conclusion

The clinical expression of OI in the Ivorian child is classical and principally governed by private mutation patterns of inheritance. This genetic disorder requires special expertise for diagnosis and treatment which must be adapted to the specific needs of the patients. The results of treatment remain poor with significant morbidity in the severe forms. While waiting for the advent biphosphonates therapies in our medical arsenal, the preventive osteosynthesis of the four limbs until skeletal maturity, appears the method of choice to limit the morbidity of this disease.

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