The relevance of a multidisciplinary care in the management of patients with Osteogenesis Imperfecta

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To the editor,

Osteogenesis imperfecta (OI) is a group of rare inherited disorders with the common feature of bone fragility and recurrent fractures. Extraskeletal manifestations can also occur, such as blue/grey sclera discoloration, dentinogenesis imperfecta, hearing loss, cardiac involvement, leading to an increased morbidity and mortality[1].

A multidisciplinary approach, with input from geneticists, pediatricians, rheumatologists, orthopedic surgeons, otorhinolaryngologists, cardiologists and other allied health care professionals, is required to recognize the full extent of organ involvement and effectively manage OI patients towards improved clinical outcomes[2,3].

We retrospectively analyzed, at our center, clinical features, treatments received and the proportion of OI patients who received multidisciplinary evaluations during the course of their disease. OI patients were selected if they had a rheumatology evaluation in the last 10 years. Multidisciplinary evaluations were defined as evaluations conducted by at least 3 physicians of different medical specialties.

A total of 31 patients with OI were included in our study, 64.5% female, with a median age at last visit of 28 years. Median age at diagnosis and median follow-up time was 2 years and 15 years, respectively. Multidisciplinary evaluations was performed in 80% of OI patients.

Type I OI had a different set of clinical manifestations when compared with other OI types (Table I). Type I OI had less bone fractures, vertebral fractures, bone deformities and need for walking aids.

No differences were found between type I and other OI types in the rate of dentinogenesis imperfecta, z-score in the first bone densitometry performed or age of last registered fracture. Family history of OI was more prevalent in type I OI (85.7% vs 42.9%, $p<0.05$).

Ear, nose and throat (ENT) involvement, mostly hearing loss, was present in 20.7% of patients. Nevertheless, 29% of patients never received an ENT evaluation. Of the 10 (32%) patients assessed through echo or electrocardiogram, 3 (30%) showed cardiac involvement.

Although OI type I had less multidisciplinary (78.3% vs 85.7%), ENT (66.7% vs 85.7%), cardiac (29.2% vs 42.9%) and genetic (54.2% vs 71.4%) evaluations than other types of OI, no statically differences were found.

Most patients (90%) received bisphosphonates at any time point during the course of their disease and 32.1% were still receiving bisphosphonates at last visit (Table I). Few patients (13.8%) were treated with drugs not usually used in OI, such as strontium ranelate.

Approximately half of patients were lost to follow-up or were discharged, especially those who remained without fractures for a time long period and/or when transitioning from pediatric to adult consultations.

Management of OI patients is complex and challenging given the rarity and heterogeneity of the disease. Best practices requires a multidisciplinary approach and regular follow-up visits throughout life, with a frequency that can vary according to age and complications[4,5].

Hearing tests, surveillance of bone deformities and bone mineral density, spirometry and echocardiograms/electrocardiograms are only some of the assessments required to fully characterize the disease extension. An early recognition of extraskeletal organ involvement allows for a timely institution of effective treatments and prophylactic measures to prevent complications and irreversible damage.

In our cohort we found less than expected routine evaluation of extraskeletal involvement and higher than expected loss of follow-up or prematurely discharged patients.

This study highlights the gaps still observed in the management of OI patients. To improve those gaps, we

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TABLE I. DEMOGRAPHIC, CUMULATIVE CLINICAL FEATURES AND TREATMENTS USED IN OSTEOGENESIS IMPERFECTA

	Whole cohort N=31	Type I OI N= 24 (77.4%)	Other types OI* N= 7 (22.6%)	P-value
Multidisciplinary evaluations - N(%)	24 (80)	18 (78.3)	6 (85.7)	0.57
ENT evaluation – N(%)	22 (71)	16 (66.7)	6 (85.7)	0.32
Cardiac evaluation – N (%)	10 (32.3)	7 (29.2)	3 (42.9)	0.40
Genetic evaluation – N(%)	18 (58.1)	13 (54.2)	5 (71.4)	0.36
First DEXA (z-score) – Mean ± SD no=23	-4.57 ± 1.9	-4.29 ± 1.6	-5.36 ± 1.2	0.25
Last DEXA (z-score) – Mean ± SD no= 22	-1.50 ± 1.7	-1.2 ± 1.2	-2.95 ± 2.7	0.29
Number of fractures - Median (IQR) no=28	7.5 (5-14.25)	6.5 (5-10.25)	17.5 (9.75-85)	<0.01
Vertebral fracture – N(%) no=29	5 (16.7)	2 (8.7)	3 (50.0)	0.05
Bone deformities - N(%) no=28	13 (44.8)	8 (34.8)	5 (83.3)	0.05
Need for walking aids – N(%) no=29	6 (20.7)	1 (4.3)	5 (83.3)	<0.01
Discoloration of the sclera – N(%) no=29	19 (65.5)	18 (78.3)	1 (16.7)	0.01
Dentinogenesis imperfecta – N(%) no=26	7 (26.9)	5 (25)	2 (33.3)	0.53
Cardiac involvement – N(%) no=22	3 (13.6)	2 (11.1)	1 (25)	0.47
ENT involvement – N(%) no=27	6 (20.7)	4 (17.4)	2 (33.3)	0.56
Bisphosphonates – N(%) no=30	27 (90)	20 (87)	7 (100)	0.43
Current bisphosphonates – N(%) no=28	9 (32.1)	5 (22.7)	4 (66.7)	0.06
Strontium ranelate – N(%) no=29	4 (13.8)	2 (8.7)	2 (33.3)	0.18
Denosumab – N(%) no=29	2 (6.9)	1 (4.3)	1 (16.7)	0.38
Loss of follow up/Discharge patients – N(%)	14 (45.2)	12 (50)	2 (28.6)	0.29

N - number; no - Number of patients with available information; ENT – Ear, nose and throat; SD - Standard deviation; IQR - Interquartile range; DEXA – Bone densitometry. P-value comparing type I OI to others type of OI. *Other types OI included 2 patients with type III OI, 1 patient with type IV OI, 1 patient with type V OI, 2 patients with type VI OI and 1 patient with type VII OI).

are developing clinical protocols to ensure multidisciplinary assessments and regular monitoring of OI patients. We expect this report can raise the awareness of the different stakeholders for the need of a multidisciplinary approach and regular monitoring of OI patients with the aim to improve their clinical outcomes, including their functionality and quality of life.

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