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CASE REPORT

Mazabraud's Syndrome: A Case Report and Up-To-Date Literature Review

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Abstract: ***Objective:*** Mazabraud's syndrome is a rare form of bone fibrous dysplasia associated with intramuscular myxomas. Fibrous dysplasia, is generally localized to pelvis and femur and it results in a fragile bone with deformities, pain, pathological fractures and functional impairment. Intramuscular myxomas, are rare benign mesenchymal neoplasms that exceptionally may evolve to malignant forms.

Methods: This case report describes a 66-year-old woman with Mazabraud's Syndrome (MS), characterized both by monostotic right femur fibrous dysplasia and by a solitary intramuscular myxoma at the right quadriceps muscle, that underwent a long-term treatment (4 years) with intravenous zoledronic acid.

Results: Zoledronic acid therapy rapidly lowered bone pain together with a reduction of intramuscular myxoma volume, but did not affect the extension of fibrous dysplasia. No adverse effects have been observed during treatment.

Conclusion: Highly active bisphosphonates are commonly used for the treatment of bone metabolic disorders and they are generally well tolerated. Zoledronic acid may represent a promising alternative to surgical intervention in MS, although its use in rare form of bone fibrous dysplasias is still controversial.

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1. INTRODUCTION

Mazabraud's syndrome (MS), a rare form of bone fibrous dysplasia (FD) associated with intramuscular myxomas (IMs), with a prevalence of 1/1,000,000 (www.orpha.net), was described by Henschen in 1926 [1] and Mazabraud in 1957 [2]. Approximately, 100 cases have been reported so far (Table **1**).

Monostotic/polyostotic FD, defined as the replacement of normal bone and bone marrow with abnormal fibrous tissue, results in fragile bones with deformities, pain, pathological fractures and functional impairment. FD generally localizes to the pelvis and femur.

IMs are rare benign mesenchymal neoplasms [3] with an incidence of 0.1-0.13/100,000 population/year that consist of undifferentiated spindle cells within the collagen fibres and myxoid stroma [4]. Although the malignant transformation of IMs is extraordinarily rare in MS (only seven cases have been reported in the literature), they may present an infiltrative pattern [5, 6].

MS often localizes in the lower limbs, and multiple myxomas are usually found inside the quadriceps muscles [5].

Here, we report a new MS case with monostotic FD in the right femur and a solitary IM in the right quadriceps muscle. Our case is peculiar in that it consists of a 4-year successful treatment of MS with intravenous zoledronate (ZOL). An up-to-date review of the literature is also presented.

2. CASE REPORT

In 2013, a 66-year-old woman presented to the University Hospital of Udine (Italy), with a diagnosis of osteoporosis (OP) (T-scores: right femoral neck = - 2.9 SD; left femoral neck = - 2.9 SD; lumbar spine = - 2.0 SD). No fractures were reported. No clinical signs, hyperfunctioning hormonal abnormalities, or skin changes (*e.g.*, café-au-lait spots) were present, but she complained of right thigh pain. She was a heavy smoker (20 cigarettes/day, for ~50 years).

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Since the DXA image of her right femur showed a somewhat "bullous" aspect, her general practitioner performed X-rays on both her limbs and Magnetic Resonance Imaging (MRI) on the upper part of her right femur, which revealed a wide medullar lesion in the proximal diaphysis (Fig. **1**).

At the baseline visit in our Unit, total-body bone scintigraphy (TBBS) demonstrated abnormal technetium Tc 99m hydroxydiphosphonate uptake in the right femoral diaphysis.

Examinations for metabolic bone diseases, including Paget's disease of bone (PDB), were negative. We diagnosed the patient with monostotic FD, and we prescribed oral cholecalciferol (2.500 IU/day) and calcium citrate (500 mg/day).

At the end of 2013, she received the first 5 mg i.v. ZOL infusion. No side effects were observed, apart from a mild one-day flu-like syndrome. Thigh pain disappeared 3-4 months after her first infusion. ZOL was repeated each January in 2015, 2016 and 2017.

In January 2015, a new MRI of the whole right femur confirmed an unchanged medullar lesion (extension of ~25 cm) with cortical swelling, suggestive of FD (Figs. **2A** and **2B**). Moreover, the scan allowed us to identify a well-defined ovoid mass, 35x25x90 mm, involving the vastus intermedius and lateralis of the right quadriceps muscle, which was hyperintense in the T2-weighted sequence and hypointense in T1-weighted sequence (Figs. **2C** and **2D**) and was referred to as IM. Consequently, a diagnosis of MS was made, even though the patient refused an IM biopsy.

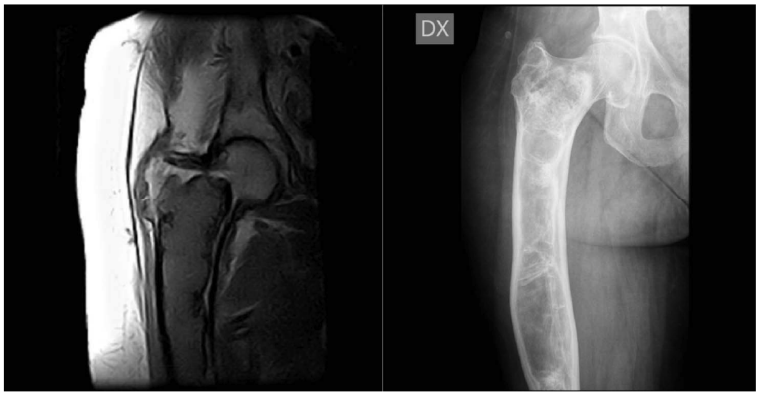

Fig. (1). Left - First RMN of the right hip. The medullar lesion arises from the trochanteric region to the diaphysis. Right - X-Rays of the right hip. The lesion has the typical appearance of FD: radiolucent, with a peculiar ground-glass appearance due to the loss of the normal trabecular pattern.

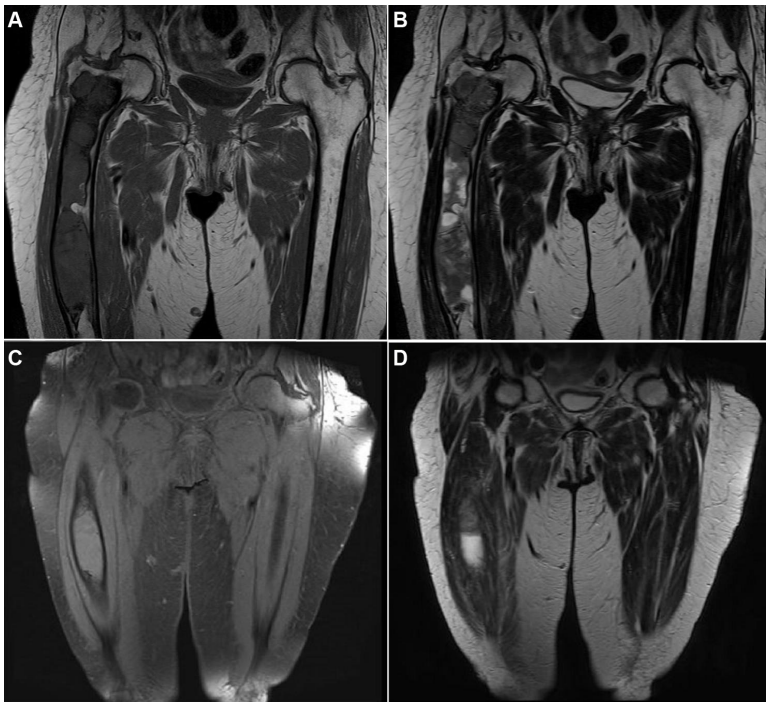

Fig. (2). (**A**): FD in T1 weighted image appears as a hypointense lesion with cortical swelling and thickness; in its 25 cm extension, it involves the femur's epiphysis and diaphysis; (**B**): FD in T2-weighted image appears as a hyperintense lesion; (**C**): IM is hypointense in T1, appearing as a well-defined ovoid lesion, with a peritumoral fat contour; (**D**): IM is hyperintense in T2- weighted image, with a visible heterogeneous contrast enhancement that reflects the hypervascular focal areas within the myxoid matrix and the fibrous septa of the lesion.

Interestingly, after the completion of ZOL therapy, the last MRI documented a reduction of the IM diameters (21x21x50 mm versus 35x25x90 mm) and stability of the femur FD.

The control TBBS in September 2017 did not show substantial changes from the previous scans; in particular, the enhanced radiotracer uptake persisted at the right femur intertrochanteric region, at the proximal and middle third of the diaphysis and at the lateral supracondylar region. The convex profile of the femoral diaphysis was unchanged. No fractures occurred during the 4-year ZOL treatment.

Before ZOL infusion, the C-Terminal telopeptide (CTX) was 0.34 ng/ml (normal values: 0.1-1); for the second, third and fourth infusions, it was 0.12, 0.08 and 0.09 ng/ml, respectively.

3. DISCUSSION

Since its first description [1], 106 cases of MS have been reported in the literature. Starting from previously published reviews [6, 7], we gathered all new cases reported in the literature by searching PubMed, Google Scholar, and Embase (Table **1**). We excluded cases where the original article could not be retrieved or cases that were lacking any information in the reviews.

MS is more common in females (68%) than males (32%). The onset of FD was known in 88 of the 105 cases. The mean age at diagnosis was 40 years, childhood onset was reported in 4 cases and the age was not given in one case. Moreover, in one MS case, FD was not detectable. Among 100 FD cases, 23 were monostotic and 77 were polyostotic (42% unilateral and 58% bilateral). In the unilateral and monostotic forms, the right side of the body was more commonly affected (57% *vs*. 43%). FD generally affects the lower limbs (83% of patients), particularly the femur (72% of monostotic disease cases). Upper limbs were involved in 41% of the cases, and other localizations were the skull and thorax (10 and 9 cases, respectively). As confirmed in the literature [6], FD develops generally 6.5 years earlier than IM develops in MS. IM developed at a mean age of 47 years, with the age at diagnosis not reported in one case. Multiple IMs were reported in 60% of cases and single IMs were reported in 40% of cases. Among the multiple IM cases, 28% were bilateral and 72% were unilateral. IMs were localized in the lower limbs in 75% of the cases (52% in the thighs), while upper limbs were involved in 22% of the cases [6]. Only in 3 cases were IMs found in the head and neck [7]. The right side of the body was involved in 61% of cases, and the left side of the body in 39%. Twenty-three patients presented with café-au-lait spots, while 10 had precocious puberty and 8 had thyroid disease. Only 7 cases developed malignant osteosarcoma at the site of pre-existing FDs (6%) [6, 7].

The aetiology of MS was not fully known until the last decade when postzygotic inactivating mutations of the *GNAS1* gene were found in cases of FD [8]. *GNAS1* encodes the alpha sub-unit of G-protein (GSα) involved in cell proliferation. Its inactivating mutations lead to aberrant cell proliferation, likely involved in FD and MS pathogenesis [9, 10], affecting the precursor cells at early stages of their commitment since bone, skeletal muscle, cartilage and adipose cells derive from a common precursor mesenchymal cell [11]. This may account for the wide range of clinical patterns: the earlier the mutation occurs, the more complex the clinical phenotype, partly explaining why MS may vary from asymptomatic to painful forms, with fractures and skeletal deformities. Interestingly, heart muscle myxomas can occur in subjects with Carney complex (OMIM #160980), which is associated with inactivating germline mutations of the *PRKAR1A* gene, which encodes a subunit of protein kinase A (*PKA*). *PKA* shares common molecular pathways with the GSα protein.

Imaging studies in MS are important for both appropriate diagnosis and follow-up to promptly recognize and treat clinical complications.

In our case, the RX-images of FD were quite clear: the femoral diaphyseal intramedullary lesions were radiolucent with a ground-glass appearance due to the loss of normal trabecular pattern and a band of surrounding sclerotic bone. Endosteal scalloping and cortical thinning were present as well. On the MRI, FD showed low intensity in the T1-weighted sequence and high intensity in the T2 weighted sequence. The surrounding sclerotic rim was hypointense in T1 and T2. FD requires radiological follow-up since malignant transformation, although rare, is possible [11]. According to the literature, baseline and control TBBSs show intense metabolic activity [12, 13].

Currently, no specific treatment for MS exists. Orthopaedic surgery may be indicated for severe cases of FD with pain, fractures and bone deformities.

Only a few studies have evaluated the long-term effects of anti-resorptive agents in FD. In our MS case, we present both the possible preventive effect of ZOL on fractures and its effect on pain reduction. Following the fourth infusion of ZOL, we were surprised by the lack of change in the control TBBS. Since radiotracer uptake may depend on several factors (*e.g*., local blood flow, osteoblastic activity and extraction efficiency) [14], it is possible that the anti-resorptive action of the cumulative ZOL dose was not potent enough to inhibit bone turnover in our patient, although the CTX decreased by almost 75% from baseline at the end of observation. Interestingly, similar results were reported with intravenous neridronate therapy in a polyostotic form of FD [15].

Generally, symptomatic IMs should be excised [11, 16]. In our patient, we were surprised by the clear reduction of the IM diameter after 4 years of ZOL treatment. Unfortunately, due to the patient's refusal, we did not perform an IM biopsy, and therefore, we cannot obtain any information on ZOL action inside the neoplastic cells. However, the observed myxoma volume reduction allows us to speculate on a possible ZOL action on IMs in MS. Of course, further biomolecular studies are necessary. Finally, ZOL in FD could act on bone pain relief, possibly improving radiological findings and bone turnover markers [17-20].

Table 1. Mazabraud's syndrome cases reported in the literature [1].

Authors	Journal	Year	Sex	Age at FD	Age at IM	Fibrous Dysplasia Characteristics				Intramuscular Myxoma Characteristics				Other
Henschen F.	Verh Dtsch Ges Pathol	1926	F	Childhood	66	Monostotic	-	Right	LL	Multiple	Unilateral	Right	LL	-
Krogius A.	Acta Chir Scand	1929	F	6	26	Polyostotic	Bilateral	-	UL/LL	Multiple	Unilateral	Right	UL/LL	-
Uehlinger E.	Virchows Archiv	1940	M	11	67	Polyostotic	Bilateral	-	Not available	Single	-	Right	LL	-
Braunwarth K.	Fortschr Geb Rontgenstr	1953	F	Not available	55	Monostotic	-	Left	Not available	Single	-	Left	-	-
Mazabraud A. and Girard J.	Rev Rhum Mal Os-teoartic	1957	M	22	54	Polyostotic	Unilateral	Right	UL/LL	Multiple	Unilateral	Right	UL	-
Heinemann G. and Worth D.	Bruns Beitr Klin Chir	1958	F	18	82	Polyostotic	Unilateral	Right	Monomelic, not available	Multiple	Unilateral	Right	Not available	
Laporte F. *et al.*	J Chir (Paris)	1961	F	12	24	Polyostotic	Unilateral	Right	Not available	Single	-	Right	-	CAL, PP, TP
Lick R.F. and Viehweger G.	Fortschr Geb Rontgenstr Nuklearmed	1962	M	18	58	Polyostotic	Bilateral	-	Not available	Multiple	Unilateral	Right	Not available	-
Mazabraud A. *et al.*	Presse Med	1967	F	Infancy	Not reported	Polyostotic	Unilateral	Left	Not available	Multiple	Unilateral	Right	Not available	CAL, PP
Roze R. *et al.*	J Radiol Electrol Med Nucl	1967	F	20	38	Polyostotic	Bilateral	-	UL/LL	Multiple	Unilateral	Right	UL/LL	CAL, MD, PP
Semat P. *et al.*	J Radiol Electrol Med Nucl	1969	M	30	47	Polyostotic	Bilateral	-	UL/LL	Single	-	Left	LL	TP
Wirth W.A. *et al.*	Cancer	1971	M	3	17	Polyostotic	Bilateral	-	UL/LL	Multiple	Unilateral	Right	UL	CAL
-	-	1971	M	18	33	Polyostotic	Bilateral	-	UL/LL, S	Multiple	Unilateral	Right	UL/LL	CAL
Lejeune E. *et al.*	Rev Rhum Mal Os-teoartic	1972	M	41	39	Polyostotic	Bilateral	-	UL/LL	Multiple	Unilateral	Right	UL/LL	CAL
Ireland D.C. *et al.*	Mayo Clin Proc	1973	F	49	49	Monostotic	-	Left	LL	Multiple	Bilateral	-	UL/LL	CAL
-	-	1973	F	59	52	Polyostotic	Unilateral	Right	LL	Multiple	Unilateral	Right	LL	-
-	-	1973	F	23	28	Polyostotic	Unilateral	Left	LL	Multiple	Unilateral	Left	LL	-
Logel R.J.	J Bone Joint Surg Am	1976	F	Childhood	41	Polyostotic	Bilateral	-	UL/LL, S	Multiple	Bilateral	-	LL, H&N	CAL, PP, TP
Berkhoff W.B. *et al.*	Ned Tijdschr Geneeskd	1981	-	-	-	-	-	-	-	-	-	-	-	-
Sedmark D.D. *et al.*	Cleve Clin Q	1983	M	33	50	Polyostotic	Unilateral	Left	LL	Single	-	Left	LL	-
Lever E.G. and Pettingale K.W.	J Bone Joint Surg Br	1983	F	1	50	Polyostotic	Bilateral	-	UL/LL	Single	-	Right	LL	PP
Segev Z. and Reiner S.	Harefuah	1985	-	-	-	-	-	-	-	-	-	-	-	-
Witkin G.B. *et al.*	Clin Orthop Relat Res	1986	M	15	40	Polyostotic	Bilateral	-	UL/LL	Single	-	Left	LL	MD
Blaiser R.D. *et al.*	Clin Orthop Relat Res	1986	F	57	55	Polyostotic	Unilateral	Left	UL/LL	Multiple	Unilateral	Left	LL, T	-
Biagini R. *et al.*	Ital J Orthop Traumatol	1987	F	10	42	Polyostotic	Bilateral	-	UL/LL	Multiple	Bilateral	-	UL/LL	-

Table (1) contd….

Authors	Journal	Year	Sex	Age at FD	Age at IM	Fibrous Dysplasia Characteristics				Intramuscular Myxoma Characteristics				Other
Glass-Royal M.C. *et al.*	Skeletal Radiol	1989	M	33	33	Polyostotic	Bilateral	-	UL, S	Single	-	Left	UL	CAL
Sundaram M. *et al.*	AJR Am J Roentgenol	1989	F	31	31	Monostotic	-	Right	LL	Single	-	Right	LL	-
Gianoutsous M.P. *et al.*	Aust N Z J Surg	1990	M	53	39	Monostotic	-	Right	LL	Multiple	Unilateral	Right	LL	-
Prayson M.A. and Leeson M.C.	Clin Orthop Relat Res	1992	F	5	36	Polyostotic	Unilateral	Right	LL, T	Single	-	Right	LL	CAL
Gober G.A. and Nicholas R.W.	Skeletal Radiol	1993	F	32	37	Monostotic	-	Left	LL	Multiple	Unilateral	Left	LL	-
Aoki T. *et al.*	Pathol Int	1995	F	37	67	Polyostotic	Bilateral	-	LL	Multiple	Bilateral	-	LL	-
-	-	1995	F	46	46	Polyostotic	Unilateral	Right	LL	Single	-	Right	LL	-
Fujii K. *et al.*	Eur J Radiol	1996	F	44	47	Polyostotic	Unilateral	Right	LL, T	Multiple	Bilateral	-	LL	-
Limouzy F. *et al.*	Rev Chir Orthop Reparatrice Appar Mot	1996	M	40	45	Monostotic		Right	LL	Single		Right	LL	-
Court-Payen M. *et al.*	Acta Radiol	1997	F	50	40	Polyostotic	Unilateral	Right	S, T	Multiple	Unilateral	Right	UL	-
Szendroi M. *et al.*	J Cancer Res Clin Oncol	1998	F	34	27	Polyostotic	Bilateral	-	UL/LL	Multiple	Bilateral	-	LL	TP
-	-	1998	F	38	54	Polyostotic	Bilateral	-	UL/LL	Multiple	Bilateral	-	LL	-
-	-	1998	F	38	54	Polyostotic	Unilateral	Left	UL/LL	Single	-	Right	LL	CAL
Cabral C.E. *et al.*	Skeletal Radiol	1998	M	44	29	Polyostotic	Unilateral	Right	UL/LL	Multiple	Unilateral	Right	LL	
Lopez-Ben R. *et al.*	Skeletal Radiol	1999	F	5	40	Polyostotic	Bilateral	-	UL/LL, S	Multiple	Bilateral	-	UL/LL	CAL, MD, PP
Thomachot B. *et al.*	Rev Rhum Engl Ed	1999	F	36	36	Polyostotic	Unilateral	Left	UL/LL	Single	-	Left	LL	CAL
Walker R.E. *et al.*	AJR Am J Roentgenol	1999	M	67	67	Monostotic	-	Right	LL	Multiple	Unilateral	Right	LL	-
Kransdorf M, Murphey M.D.	Radiology	1999	F	34	34	Polyostotic	Unilateral	Right	LL	Single	-	Right	LL	-
Okamoto S. *et al.*	Virchows Arch	2000	F	17	52	Polyostotic	Bilateral	-	Not reported	Multiple	Bilateral	-	Not reported	TP
-	-	2000	F	34	27	Polyostotic	Bilateral	-	LL	Multiple	Bilateral	-	LL	-
-	-	2000	F	38	55	Polyostotic	Unilateral	Left	Not reported	Single	-	Left	LL	CAL
Struk D.W. *et al.*	Can J Surg	2000	F	49	53	Monostotic	-	Right	LL	Single	-	Right	LL	-
Faivre L. *et al.*	Am J Med Genet	2001	M	18	42	Polyostotic	Bilateral	-	UL/LL	Multiple	Bilateral	-	LL	-
-	-	2001	F	35	35	Polyostotic	Bilateral	-	UL/LL	Multiple	Bilateral	-	UL/LL	CAL, TP
Delabrousse E. *et al.*	J Radiol	2001	F	40	40	Monostotic	-	Right	LL	Multiple	Unilateral	Right	LL	-
Pollandt K. *et al.*	Pathologe	2002	F	Before IM	42	Polyostotic	Unilateral	Left	LL	Multiple	Unilateral	Right	LL	-
Iwasko N. *et al.*	Skeletal Radiol	2002	F	39	24	Polyostotic	Unilateral	Left	LL	Multiple	Unilateral	Left	LL	-
-	-	2002	F	Before IM	39	Polyostotic	Bilateral	-	LL, S	Multiple	Bilateral	-	LL	CAL

Table (1) contd….

Authors	Journal	Year	Sex	Age at FD	Age at IM	Fibrous Dysplasia Characteristics				Intramuscular Myxoma Characteristics				Other
-	-	2002	F	Before IM	63	Polyostotic	Unilateral	Right	LL	Single	-	Left	LL	-
-	-	2002	F	52	52	Polyostotic	Unilateral	Right	LL, T	Multiple	Unilateral	Right	LL	-
-	-	2002	M	49	49	Monostotic	-	Left	LL	Multiple	Unilateral	Left	LL	-
-	-	2002	F	65	65	Polyostotic	Unilateral	Right	UL	Single	-	Right	UL	-
-	-	2002	F	56	56	Polyostotic	Unilateral	Right	UL	Single	-	Right	UL	-
Tsitourdis I. *et al.*	Eur J Radiol Extra	2002	F	5	28	Polyostotic	Bilateral	-	UL/LL, S, T	Single	-	Right	LL	CAL, PP
Fang A.S. *et al.*	Clin Orthop Relat Res	2003	M	Childhood	33	Polyostotic	Unilateral	Right	LL	Single	-	Right	LL	-
Fertikh D.	Appl Radiol	2003	F	59	59	Polyostotic	Bilateral	-	Not reported	Multiple	Unilateral	Left	LL	CAL, PP, TP
Jahla D.N. *et al.*	Hum Pathol	2003	F	44	44	Polyostotic	Unilateral	Right	UL	Multiple	-	Right	UL	CAL, MD
Kabukcouglu F. *et al.*	Pathol Oncol Res	2004	F	52	52	Polyostotic	Unilateral	Left	LL	Single	-	Left	LL	-
Muthukumar T. *et al.*	Osteologiai Kö zlemén yek	2005	M	Before	37	Polyostotic	Unilateral	Right	UL	Multiple	Unilateral	Right	UL	-
Nguyen B.D. *et al.*	Clin Nucl Med	2005	M	48	48	Polyostotic	Unilateral	Right	UL	Multiple	Unilateral	Right	UL	MD
Endo M. *et al.*	Skeletal Radiol	2006	M	64	64	Monostotic	-	Right	LL	Single	-	Right	LL	-
-	-	2006	F	64	60	Monostotic	-	Right	LL	Single	-	Right	LL	-
Zoccali C. *et al.*	Int Orthop	2009	F	32	32	Polyostotic	Unilateral	Right	LL	Single	-	Right	LL	CAL
Myake M. *et al.*	Clin Nucl Med	2006	M	64	64	Monostotic	-	Right	LL	Single	Unilateral	Right	LL	-
Martin B. *et al.*	Eur Radiol	2007	F	52	52	Polyostotic	-	Left	LL	Multiple	Unilateral	Left	LL	-
McLaughlin A. *et al.*	AJR Am J Roentgenol	2007	F	53	53	Polyostotic	Unilateral	Left	UL	Single	-	Left	UL	-
Singnurkar A. *et al.*	Skeletal Radiol	2007	M	Before 42	42	Polyostotic	Bilateral	-	UL/LL, S	Multiple	Unilateral	Left	LL	-
Calisir C. *et al.*	Korean J Radiol	2007	F	65	55	Monostotic	-	Left	LL	Multiple	Unilateral	Left	LL	-
MacFarlane P. *et al.*	Eur J Surg Oncol	2007	M	20	45	Polyostotic	Bilateral	-	LL, T	Multiple	Bilateral	-	LL	-
Schepers S. *et al.*	URL: http://www.eurorad.org/case.php?id=6532	2008	M	35	33	Polyostotic	Bilateral	-	UL	Single	-	Right	UL	-
Santos C.T. *et al.*	Orbit	2008	M	48	48	Polyostotic	Unilateral	Right	S	Single	Unilateral	Right	H&N	-
Zhao H. *et al.*	Lin Chuang Yu Bing Li Xue Za Zhi	2008	F	60	60	Monostotic	-	Right	LL	Single	Unilateral	Right	LL	-
Beele X. *et al.*	Journal of the Belgian Society of Radiology	2008	-	-	-	-	-	-	-	-	-	-	-	-
Tagliafico A. *et al.*	J Ultrasound Med	2009	F	40	40	Monostotic	-	Left	LL	Multiple	Unilateral	Left	LL	CAL, PP

Table (1) contd….

Authors	Journal	Year	Sex	Age at FD	Age at IM	Fibrous Dysplasia Characteristics				Intramuscular Myxoma Characteristics				Other
Crawford E.A. *et al.*	J Bone Joint Surg Am	2009	M	63	-	Polyostotic	Unilateral	Right	UL	Multiple	Unilateral	Right	UL	MD
Tang J. *et al.*	Zhonghua Bing Li Xue Za Zhi	2009	-	-	-	-	-	-	-	-	-	-	-	-
Arishima Y. *et al.*	J Orthop Sci	2010	F	71	71	Monostotic	-	Left	LL	Single	-	Left	LL	-
Case D.B. *et al.*	Radiograph-ics	2010	F	69	69	Polyostotic	Unilateral	Left	LL, T	Single	-	Left	LL	-
Ijpma F.F. *et al.*	Ned Tijdschr Geneeskd	2010	F	51	51	Polyostotic	Bilateral	-	LL	Single	-	Left	LL	-
Kitagawa Y. *et al.*	J Orthop Sci	2011	F	49	45	Polyostotic	Bilateral	-	UL/LL	Multiple	Bilateral	-	UL/LL	CAL
Van der Wal W.A. *et al.*	J Med Case Reports	2011	F	Before	49	Polyostotic	Unilateral	Left	LL	Multiple	Unilateral	Left	LL	-
Yang X.D. *et al.*	Zhonghua Bing Li Xue Za Zhi	2011	-	-	-	-	-	-	-	-	-	-	-	-
Gaumetou E. *et al.*	Orthop Traumatol Surg Res	2012	M	42	42	Polyostotic	Bilateral	-	LL, T	Multiple	Bilateral		LL	-
Schimmoller L. *et al.*	Radiologe	2012	F	40	40	Polyostotic	Unilateral	Left	UL	Multiple	Unilateral	Left	UL	-
John A.M. *et al.*	Indian J Endocrinol Metab	2013	F	25	18	Polyostotic	Bilateral	-	UL/LL	Multiple	-	Left	LL	-
Munskgaard P.S. *et al.*	Acta Radiol Short Rep	2013	F	54	54	Polyostotic	Unilateral	Right	LL	Multiple	Unilateral	Right	LL	-
Tsourdi E. *et al.*	J Clin Endocrinol Metab	2013	F	45	45	Polyostotic	Bilateral	-	LL	Single	-	Not reported	UL	CAL
Fu S. *et al.*	Oncology Letters	2014	M	38	38	Monostotic	-	Left	S	Single	-	Left	H&N	-
Wan J. *et al.*	Indian Journal of Orthop	2014	F	44	44	Monostotic	Unilateral	Right	UL	Single	-	Right	UL	-
Perez-Sanchez P. and Gonzáles-Llorente J.	Radiología	2014	M	87	87	Polyostotic	Unilateral	Right	UL	Multiple	Unilateral	Right	UL	-
Szymanski C. *et al.*	Orthop Traumatol Surg Res	2015	F	51	45	Monostotic	Unilateral	Left	LL	Multiple	-	Left	LL	MD
Brescia L. *et al.*	Rev Med Liege	2015	F	24	38	Polyostotic	Unilateral	Right	UL/LL, T	Multiple	Bilateral	-	LL	-
Alhujayry A.K. *et al.*	Ann Med Surg (Lond)	2015	M	24	18	Polyostotic	Unilateral	Left	LL	Single	-	Left	LL	-
Samper Wamba J.D. *et al.*	Indian J Radiol Imaging	2015	F	69	69	Polyostotic	Unilateral	Right	LL	Multiple	Unilateral	Right	LL	-
Piciu D. *et al.*	BMC Endocr Disord	2015	M	57	57	Polyostotic	Unilateral	Left	LL, T	Single	-	Left	UL	TP

Table (1) contd….

Authors	Journal	Year	Sex	Age at FD	Age at IM	Fibrous Dysplasia Characteristics				Intramuscular Myxoma Characteristics				Other
Granel-Villach L. *et al.*	Cir Cir	2016	F	Not yet	40	NOT YET				Multiple	Unilateral	Right	LL	-
Schwarze M. *et al.*	Der Orthopäde	2017	F	47	47	Polyostotic	Unilateral	Right	LL	Multiple	Unilateral	Right	LL	PP
Cox J.L. *et al.*	Virchows Archiv	2017	F	43	43	Polyostotic	Unilateral	Left	LL	Multiple	Unilateral	Left	LL	-
-	-	2017	M	66	56	Monostotic	-	Left	LL	Multiple	Unilateral	Left	LL	-
Our Case	-	**2017**	**F**	**66**	**66**	**Monostotic**	**Unilateral**	**Right**	**LL**	**Single**	**Unilateral**	**Right**	**LL**	-

[1]All available articles were downloaded. The Authors translated and read all the papers written in the following languages: English, Spanish, German, French and Dutch. Data from very old or online unavailable papers together with those written in Chinese or Hebrew (Zaho H *et al*., Tang J *et al*., Yang XD *et al*., Segev Z *et al*.) were derived by formerly published reviews.

LL = lower limb, UL = upper limb, UL/LL = upper and lower limbs, S = skull, T = thorax, H&N = head and neck, TP = thyropathy, PP = precocious puberty, CAL = cafè-au-lait spots, MD = malignant degeneration.

CONCLUSION

Currently, highly active bisphosphonates are available for common bone metabolic disorders and they are generally well tolerated [21-23]. These drugs may become a promising alternative to surgical intervention in MS, but standardized therapeutic protocols and controlled clinical trials are required to determine whether they can truly control disease progression.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. All human procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

STANDARD OF REPORTING:

CARE guidelines and methodologies have been followed.

CONSENT FOR PUBLICATION

Consent was obtained from the patient for publication of this report and any accompanying images.

FUNDING

None.

CONFLICT OF INTEREST

Authors declare no conflict of interest, financial or otherwise.

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