FRAGILITY FRACTURES AS THE INITIAL MANIFESTATION OF INDOLENT SYSTEMIC MASTOCYTOSIS

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INTRODUCTION

Systemic mastocytosis (SM) is a rare disease (2 cases per 100.000 population/ year) characterized by clonal proliferation of abnormal mast cells in several tissues, most often skin and bone marrow. Indolent systemic mastocytosis (ISM) is the commonest disease variant in adults, characterized by very low rate of mast cell proliferation. SM has been recognized as a cause of secondary osteoporosis.

OBJECTIVE

To evaluate bone mineral density and fragility fractures in ISM patients.

METHODS

Fourteen patients (9 women, 7 premenopausal), aged 27-63 years, diagnosed with ISM according to World Health Organization criteria (2008) were studied retrospectively.

Clinical examination, biochemical evaluation and bone mineral density (BMD) measurements by dual-energy X-ray absorptiometry at the lumbar spine (L_1-L_4), the total proximal femur, the femoral neck and the distal one-third radius were performed.

T-score was used to define osteopenia (<-1 to >-2.5 SD) or osteoporosis (-2.5 SD or lower) in postmenopausal women or men aged 50 years or older, and z-score ≤−2.0 for low BMD in younger men and premenopausal women, according to the guidelines of International Society for Clinical Bone Densitometry. Fractured vertebrae were excluded from BMD measurement.

No patient reported other diseases or use of treatments known to affect bone or mineral metabolism, at initial assessment.

Table 1: Clinical characteristics of ISM patients.

Patient No	Sex	Age (*) (*years*)	BMI (*Kg/m²*)	Smoking	Alcohol intake	Main symptom for SM investigation
1	F	41	23.4	Yes	Minimal	Urticaria pigmentosa
2	F	31	23.7	Yes	Minimal	Urticaria pigmentosa
3	F	56	30.8	No	Minimal	Skin lesions
4	F	43	33.5	Yes	Minimal	vertebral fracture
5	F	27	22.3	No	Minimal	Urticaria pigmentosa
6	F	63	24.9	Yes	Minimal	Drug anaphylaxis
7	F	41	31.2	No	No	Urticaria pigmentosa
8	F	45	31.6	Yes	No	Anaphylactic shock
9	F	31	23.5	Yes	Minimal	Rib fractures
10	M	38	26.6	Yes	Minimal	Vertebral fracture
11	M	57	31.2	Yes	Minimal	Urticaria pigmentosa
12	M	37	26.3	No	Minimal	Food anaphylaxis
13	M	45	39.0	No	Minimal	Skin lesions
14	M	53	31.5	No	Minimal	Urticaria pigmentosa

(*) Age at initial bone mineral density evaluation

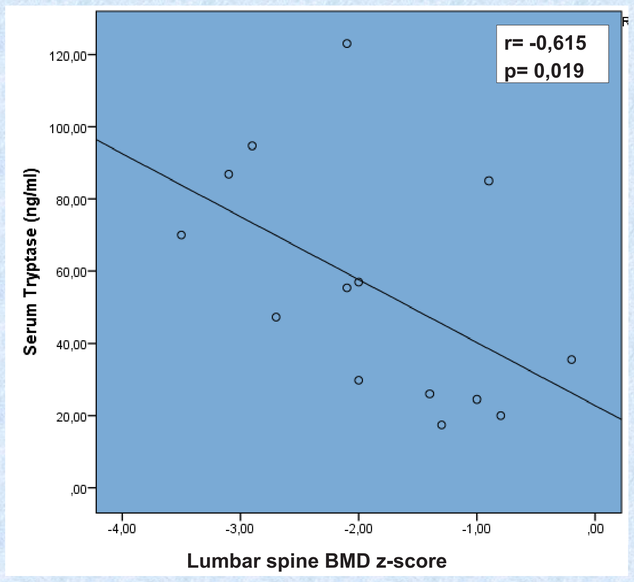
RESULTS

- Three patients (21.4%) had fragility fractures: a 43-year-old premenopausal woman (*patient No 4*) & a 38-year-old man (*patient No 10*) had vertebral fractures, while a 31-year-old premenopausal woman (*patient No 9*) had non-vertebral fractures (Table 1).
- Fragility fractures were the cause for SM investigation since none of these patients had cutaneous mastocytosis and only 1 patient reported a mild episode of anaphylaxis, at diagnosis (Table 1).
- $25(OH)D_3$ deficiency (<20ng/ml) was detected in 7 patients (50%) (Table 2) .
- Bone densitometry showed osteoporosis in 2 patients (14.3%), osteopenia in 2 (14.3%) and low BMD in 7 (50%) (Table 3). BMD z-score was generally lower at the spine than at the hip and at the femoral neck (all patients) (p<0.001).
- Serum tryptase levels were negatively correlated (r= -0,615, p= 0,019 with lumbar spine BMD z-score (all patients) (Figure 1).

Table 2: Laboratory characteristics of ISM patients.

No	tryptase (*ng/ml*)	PTH (*pg/ml*)	Ca serum (*mg/dl*)	P serum (*mg/dl*)	creatinine (*mg/d*l)	Albumin (*mg/d*l)	25(OH)D_3 (*ng/ml*)	ALP (*U/L*)	TSH (*μIU/ml*)	Testo (*mg/dl*)
1	29.8	24	9.3	3.3	0.8	4.1	24.3	54	0.4	
2	20	37.4	8.8	3.4	0.5	4.2	19.1	57	1.9	
3	123	43	9.2	4.4	0.7	4.7	30.4	69	3.2	
4	47.3	32	9.5	3	0.7	4.3	22.3	66	1.4	
5	86.8	40,2	9.3	4.6	0.7	4.8	19.8	78	1.7	
6	24.5	48.4	9.2	3.9	0.7	4.3	20.8	64	1.1	
7	57	38.2	9.3	2.5	0.6	3.9	9	95	1.3	
8	94.7	21	9.4	3.7	0.7	4	17.7	65	1.2	
9	17.4	24	9.1	4.3	0.6	4.3	28	55	1.8	
10	70	34	9.2	3.1	1.1	4.7	27.7	92	1.2	330
11	85	49	9.4	3.2	1	4.5	30	104	1.2	339
12	35.5	31	9.5	4.2	0.8	4.9	12.5	62	1.8	425
13	55.4	26.7	10.1	3.4	0.9	4.6	18.2	91.6	2.4	496
14	26	33	10.2	4.1	1	4.8	16.7	81	0.8	446

Figure 1: Correlation between serum tryptase levels & LS BMD z-score



Spearman correlation analysis

Table 3: Fracture history and BMD of ISM patients.

No	Non Frag fractures	Frag fractures	LS BMD (*) z/T-score	T Hip BMD z/T-score	FN BMD z/T-score	1/3 radius BMD z/T-score
1	0	0	z -2.1	z 0.6	z -0.2	z 1.5
2	left forearm	0	z -0.8	z -0.1	z -0.4	z -0.1
3	left forearm	0	T -3.4	T 0.1	T 0.3	T -2.3
4	0	vertebral fracture (L4)	z -2.7	z -0.8	z 0.2	z 1.1
5	0	0	z -3.1	z -0.9	z -1.1	z -0.8
6	0	0	T -2.6	T -1.6	T -2.0	T -0.1
7	0	0	z -2.1	z -0.5	z -0.8	z 1.1
8	pelvis, right forearm	0	z -2.9	z -1.3	z -1.9	z 0.3
9	right forearm	Rib fractures	z -1.3	z -0.8	z -1.6	z -0.3
10	0	vertebral fracture (L5)	z -3.5	z -0.9	z -1.4	z -0.3
11	0	0	T -1.6	T -0.6	T -1.5	T -0.1
12	0	0	z -0.2	z -0.5	z -1.2	z 0.1
13	0	0	z -2.2	z 0.3	z 0.5	z -0.1
14	vertebral fracture (L2)	0	T -1.8	T -1.3	T -1.2	T -1.9

Frag fractures: fragility fractures, LS: lumbar spine (L1-L4), T Hip: total hip, 1/3 radius: distal one-third radius, denotes osteoporosis, denotes osteopenia, denotes low bone mass

(*) *Fractured vertebrae were excluded from BMD measurement.*

CONCLUSION

Bone involvement is frequent in ISM patients and may be the initial manifestation. Osteoporotic fractures of unknown aetiology should lead to the suspicion of SM particularly in individuals younger than 50 years.

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