Heterogenous Histology in Atypical Femoral Fractures without Bisphosphonate Treatment: A Case Series Comparing Bisphosphonate Treated with Untreated Patients

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INTRODUCTION:

Atypical femoral fractures (AFF) are a rare type of insufficiency fracture with a strong association to antiresorptive treatment (ART). Little attention has been given to patients with verified AFF and no reported use of ART. Differences in the histological picture of the fracture site in patients with and without ART treatment might provide important insights into the underlying pathophysiology.

METHODS:

Between 2008 and 2020, 16 patients with surgically treated AFF underwent surgical resection of the stress fracture lesion using a cylindrical bone drill (Figure 1). Of the 16 patients, 9 patients (all incomplete, 5 women) had no reported exposure to ART (-ART group) (mean age 70.5 years, SD 11.8 years). Of the remaining 7 patients (mean age 76.7 years, SD 9.3 years) with ART treatment (+ART group), 3 were incomplete (3 women) and ART treatment was given for on average 10.7 years, (SD 8.9 years). While the common mechanism for AFF in the +ART group was long-term bisphosphonate treatment, there was a variety of possible mechanisms in the -ART group (Mb Paget N=1, adynamic bone disease N=1, hypophosphatasia N=1, severe Coxa vara N=1, extensive lateral bow N=1, unspecified N=4). Fractures in the mid-shaft region, compared to the subtrochanteric region, were more frequent in -ART (N=6) compared to +ART (N=3) and multiple cortical lesions were only seen in the -ART group (N=4).

RESULTS:

The width of the fracture gap was similar in the two groups; -ART group, mean 297 mm (SD 191.2) compared to the +ART group, mean 152.8 mm (SD 31.2), 95 % CI -361.0 to 72.4; (p= 0.17). The bone volume fraction (BV/TV) was lower in the -ART group, mean 72% compared to the ART group, mean 85%; 95% CI 6.0 to 19.98; (p= 0.0014). The specific surface of bone (BS/TV) was similar between groups; 44.8% in the -ART group compared to 54.2% in the ART group; 95% CI, -8.8 to 27.6. Percentage of alive osteocytes was similar, mean 39.87% (SD 9.03) in the -ART group compared to mean 39.2% (SD 16.08) in the +ART group. After surgical fixation all incomplete fractures healed uneventfully.

DISCUSSION AND CONCLUSION:

The majority of patients without ART in our study had an underlying bone metabolic disease which most likely caused the insufficiency fracture. These findings are supported by differences in radiological and histological findings. For a successful orthopaedic treatment of patients with AFF with and without ART, a high level of suspicion for underlying bone metabolic pathologies or predisposing biomechanical variations is necessary.

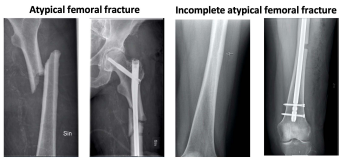

Figure 1: Atypical femoral fracture before and after internal fixation and drill biopsy and incomplete femoral fracture before and after internal fixation and drill biopsy.

Table 1: Background information and radiological findings.

	-ART (N=9)	+ART (N=7)
Mean age in years (SD)	70.5 (SD 11.8)	76.7 (SD 9.3)
Women	5	7
Treatment with ART for osteoporosis	0 (1 patient received a single dose of Aclasta® for Mb. Paget)	7 of 7
Incomplete AFF	9 (5 women)	3 (3 women)
Fracture	Shaft: 6 Subtrochanteric: 3	Shaft: 3 Subtrochanteric: 3 (Proximal shaft: 1)
Bilateral AFFs	2	1
Multiple lesions	4	0
Potential pathomechanism	Mb Paget N=1 Adynamic bone disease N=1 Hypophosphatasia N=1 Severe coxa vara N=1 Extensive lateral bow N=1 Unspecified N=4	Prolonged exposure to ART