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IMPACT OF VERTEBRAL FRACTURE ON AUXOLOGICAL PROFILE AND INSULIN-LIKE GROWTH FACTORS OF CHILDREN AFTER ACUTE LYMPHOBLASTIC LEUKEMIA TREATMENT

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INTRODUCTION

Children with acute lymphoblastic leukemia (ALL) often experience diverse skeletal complications following the treatment. Vertebral fracture (VF) is the hallmark of osteoporosis and have been recognized as a major skeletal complication of ALL. VF are frequently asymptomatic, thereby undetected in the absence of routine surveillance and its severity is related to the height decline[1, 2]. Insulin-like growth factor-1 (IGF-1) is a critical mediator of bone growth while its concentration is lower in osteoporotic patients[3].

AIM

This study aimed to investigate the overall prevalence of VF following childhood ALL treatment and examine the height trajectory and insulin-like growth factors in association with the presence of VF.

METHOD

One hundred and seventy-two children (59.3 %, male) who were diagnosed with ALL at age between 2 and 18 years visited endocrinology clinic following the treatment completion (baseline) were screened for lateral thoracolumbar spine radiographs for VF detection (interpretation by using semi-quantitative method)[3]. Anthropometric measurements were obtained at three time points: at leukemia diagnosis (LD), treatment completion (TC), and 12 months after TC. The association of IGF-1 and insulin-like growth factor binding protein-3 (IGFBP-3) with the presence of VF were examined.

RESULTS

Mean age at ALL diagnosis was 6.5±3.4 years with treatment duration of 4.0±1.8 years (**Table 1**). Mean height and body mass index *Z*-score of study subjects at baseline was -0.1±1.0 and 0.3 ±1.4. respectively. Thirty-five children (20.3 %) had VF at baseline, and among those with VF, 97.1 % had either mild or moderate deformity. 5th lumbar vertebrae was the most frequently injured site (20.0 %). Median lumbar spine bone mineral density *Z*-score was -1.0 (Interquartile range of -1.6 and -0.8) in children with VF. Baseline *Z*-scores for height and weight were lower in children with VF than without VF while height *Z*-scores in children with VF had greater height decline than without VF (0.5±0.6 and 0.2±0.8; *P*=0.02) (**Figure 1**). Children with VF had lower IGF-1 and IGFBP-3 *Z*-scores than without VF at TC (**Table 2**). Decrease in IGF-1 level was associated with the presence of VF (**Table 3**).

Clinical Parameters	Results(n=172)
Demographic data	
Age	
Baseline, y	10.3±3.4
At ALL diagnosis, y	6.3±3.4
Male, n (%)	102 (59.3)
Leukemia characteristics	
Classification	
Pre-B-cell	164 (95.3)
T-cell	7 (4.1)
Biphenotype	1 (0.6)
Treatment	
Duration, y	4.0±1.8
Chemotherapy only (%)	139 (80.8)
Chemotherapy + Transplantation (%)	33 (19.2)
Anthropometry	
Height *Z*-score	-0.1±1.0
Weight *Z*-score	0.2±1.2
BMI *Z*-score	0.3±1.4
VF assessment	
VF, n (%)	35 (20.3)
Mild or moderate deformity, n (%)	24 (97.1)
Most frequent location, vertebra (%)	L5 (20.0)
DEXA, n (%)	19 (9.1)
LSBMD *Z*-score, median (IQR)	-1.0 (-1.6, -0.8)

Table 1. Description of the Cohort at Baseline

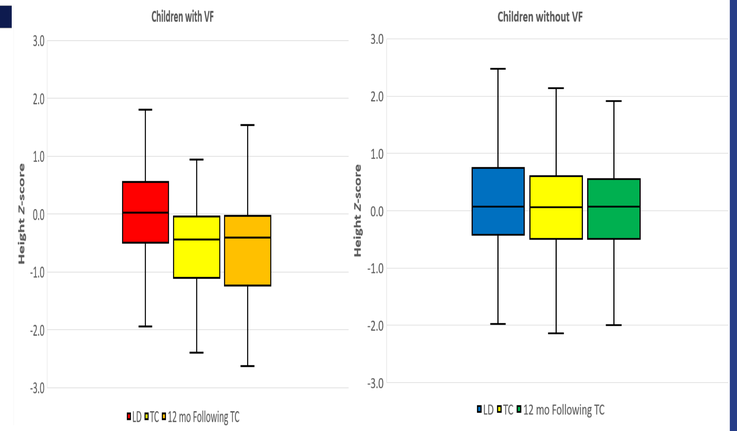

Figure 1. Height Z-scores of Children with VF from Pre- to Post-treatment

	With VF (n=35)	Without VF (n=137)	*P*
At TC			
IGF-1 *Z*-score	-1.2±1.0	0.0±0.8	*<0.01*
IGFBP-3 *Z*-score	-2.3±1.1	-1.3±1.0	*<0.01*
12 months following TC			
IGF-1 *Z*-score	-1.2±0.9	-0.3±0.8	*<0.01*
IGFBP-3 *Z*-score	-1.6±0.9	-0.9±0.9	*<0.01*

Table 2. Comparison of IGF-1 and IGFBP-3 in Children With and Without VF

	OR (95 % CI)	*P*
At TC		
Height *Z*-score	0.7 (0.4-1.4)	*0.37*
IGF-1 *Z*-score	0.3 (0.2-0.5)	*<0.01*
IGFBP-3 *Z*-score	0.7 (0.4-1.1)	*0.12*

Table 3. Association of IGF-1 and IGFBP-3 with the Presence of VF

CONCLUSIONS

Substantial number of children encountered VF once ALL treatment was completed and the presence of VF might lead to compromised auxological state, prominent height decline and IGF-1 deficiency. Routine VF surveillance at pre- and post-treatment, is critical for the prevention of future VF incidence.

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