

Introduction

- Chronic nonbacterial osteomyelitis (CNO) is a rare autoinflammatory disease affecting bone predominantly affecting children
- CNO is characterized by relapsing episodes of localised bone inflammation
- This results in pain, swelling and loss of function
- It may affect one or multiple sites and often follows a relapsing-remitting course
- The genetic basis for sporadic CNO is poorly understood
 - associations with FBLIM1, FGR and an IL-10 promoter region have been found but are inconsistent between cohorts
- Psoriasis, inflammatory bowel disease and spondyloarthritis are frequent co-morbidities
 - HLA alleles are associated with these co-morbidities in the general population
- No HLA association has been demonstrated in CNO

Aim

- To determine the frequency of HLA class I alleles in an Irish cohort of patients with CNO compared to Irish population frequencies

Methods

- Whole exome sequencing was performed on blood
- HLA alleles were predicted from whole exome sequencing results using Optitype software through the Nextflow nf-core/hlatyping pipeline (version 1.1.5)
- Comparison was made with previously published Irish HLA allele frequencies
- Statistical analysis was performed in RStudio (version 1.1.456).

HLA class I frequencies in Irish CNO cohort compared to general population

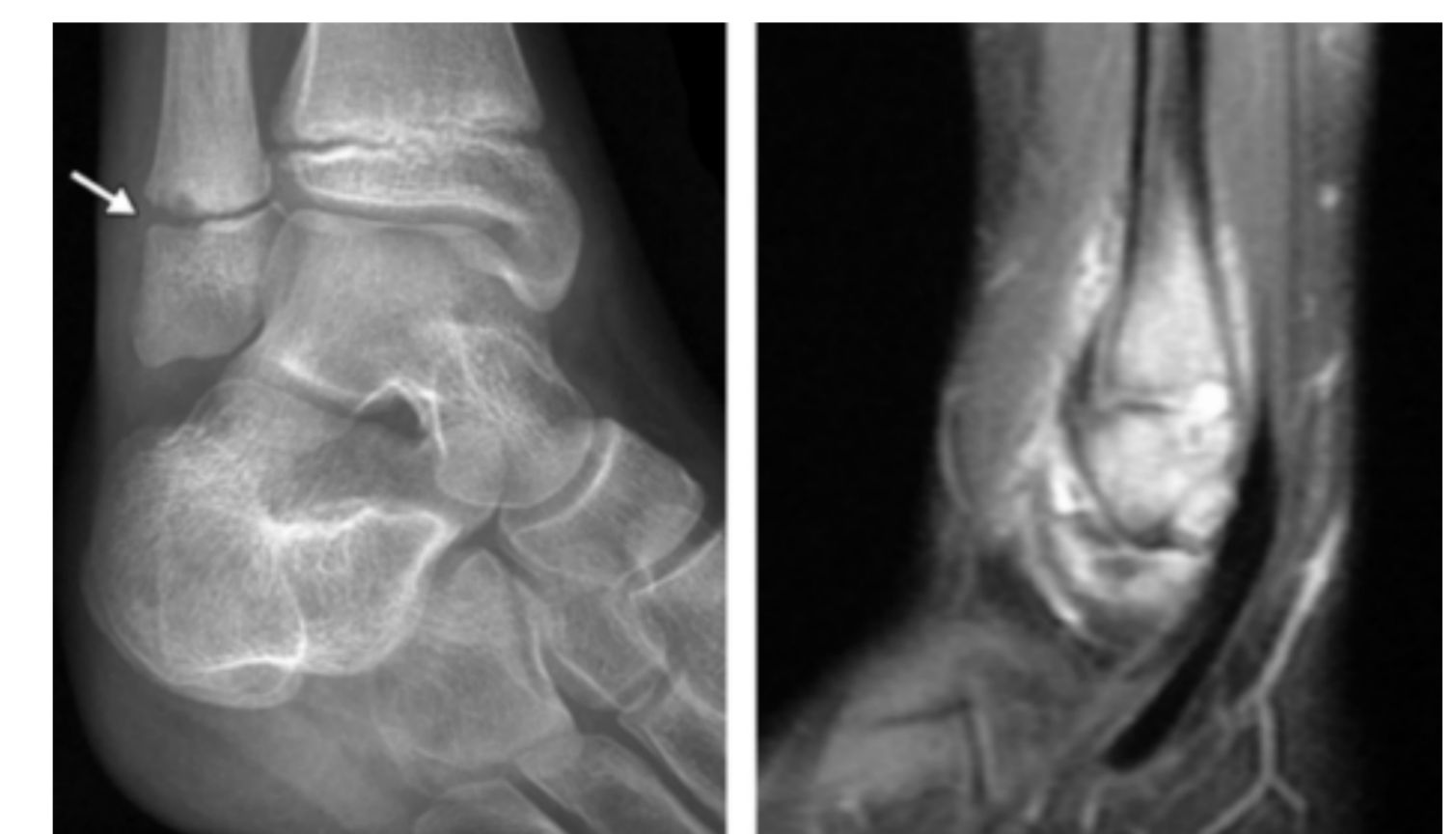
HLA Class I allele	CNO frequency	Irish population frequency	Odds ratio (95% confidence interval)
B*27:05	17.5%	6%	3.28 (1.18 – 7.8) p = 0.011
C*06:02	27.5%	17.5%	1.96 (0.079 – 3.74) p = 0.13

Results

- HLA class I prediction was successful in all 43 participants
- Co-morbidity with HLA-B*27 associated diseases occurred with the same frequency in those carrying the allele as in the overall cohort
- HLA-C*06:02 occurred at the same frequency in patients with and without psoriasis
- All other class I alleles were found at frequencies close to the Irish population frequency

Conclusions

- Chronic nonbacterial osteomyelitis is associated with HLA-B*27:05 in the Irish population



Typical appearance of CNO on x-ray (left) and MRI (right)

Clinical characteristics (n = 43)

Characteristic	Number (%)	Median (range)
Female	32 (74.4)	
Age at onset		9.2 years (3.1-14.3)
Age at diagnosis		10.5 years (5.9-15.5)
Unifocal disease	4 (9.3)	
Extrasosseous involvement:		
• Arthritis	9 (20.9)	
• Psoriasis	9 (20.9)	
• Pustulosis	4 (9.3)	
• Aphthous ulceration	4 (9.3)	
• Severe acne	2 (4.6)	
• Pyoderma gangrenosum	2 (4.6)	
• Hidradenitis suppurativa	1 (2.3)	
• Inflammatory bowel disease	1 (2.3)	
Family history:		
• Psoriasis	19 (44.2)	
• Inflammatory bowel disease	7 (16.2)	
• Inflammatory arthritis	9 (20.9)	

References

- Girschick H, *et al* (2018) The multifaceted presentation of chronic recurrent multifocal osteomyelitis: a series of 486 cases from the Eurofever international registry. *Rheumatology*.
- Wipff J, *et al* (2015) A large national cohort of French patients with chronic recurrent multifocal osteitis. *Arthritis Rheumatol*.
- Winchester R, *et al* (2012) HLA associations reveal genetic heterogeneity in psoriatic arthritis and in the psoriasis phenotype. *Arthritis Rheum*.
- Dunne C, *et al* (2008) HLA-A, B, Cw, DRB1, DQB1 and DPB1 alleles and haplotypes in the genetically homogenous Irish population. *Int J Immunogenet*.