acid excretion and creatinine clearance was low, being 290 mg/day and 37 mL/min respectively. Additional abnormal investigations included a haematocrit of 27.3%, urea of 30 mg/dl, ESR of 78 mm/h. Serum triglyceride and total lipid were elevated being 291 mg/dl and 1281 mg/dl respectively. On USG bilateral soft tissue swelling in the axillar region were found to be compatible with lipomatosis. Urolithiasis was not observed. With these findings and family history she was suspected to have hereditary familial hyperuricemic nephropathy.

After resolution of the acute attack with indomethacin, allopurinol treatment was started but had to be discontinued upon occurrence of widespread erythematous rash. She was hospitalised and desensitisation regime lasting 10 days was commenced. After desensitisation, she was free of symptoms with 300 mg/day allopurinol and 0.5 mg/day colchicine. Four months later, she developed oral ulcers. Since there was a doubtful genital ulcer history she was examined for Behçet's disease. Pathergy test was negative and unexpectedly she was HLA B27 positive but no other signs suggesting spondyloarthropathy was present. Oral ulcers disappeared after allopurinol dosage has been lowered to 150 mg/day, the rash or ulcers has not recurred. The tophi were dissolved, renal functions and blood pressure have not deteriorated over time, there has been dramatic improvement of her symptoms with normalisation of serum urate levels, she is now Steinbrocker class II.

Results

Conclusion Hyperuricemia or gout appearing at an early age in a female is usually associated with progressive renal failure. Early recognition of this disorder is important since allopurinol therapy may ameliorate the progression of the renal lesion. In cases of hypersensitivity to allopurinol oral desensitisation is a feasible approach.

AB0156 THE EFFICACY OF ALENDRONATE IN POSTMENOPAUSAL OSTEOPOROSIS

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Background This is a prospective study of bone mineral density in postmenopausal women treated with alendronate.

Objectives To evaluate the efficacy of alendronate in postmenopausal osteoporotic women for 1, 2 and 3 years.

Methods In a prospective study, we included 98 women diagnosed of postmenopausal osteoporosis attended from 1997 to 2000. The mean age was 59.07 (SD: 6.68). Patients received alendronate 10 mg daily, they were allowed to take calcium and vitamin D supplementation. The subjects were assessed at baseline, 12, 24 and 36 months for bone mineral density (BMD) measurements and X-ray and every 6 months blood and urinary biochemistries and markers of bone turnover were done.

Results Sixteen patients (16%) have dropped out because of adverse effects, the most common was gastrointestinal events. 34 (34.6%) patients had previous fractures (17 had spine fractures, 12 Colles's fractures and one hip fracture). Three patients on treatment with alendronate had new fractures (1 spine, 1 scaphoid and one Colles's fracture). 70, 24 and 7 subjects have completed one, two and three years of treatment, respectively. The results were analysed by Student's t-test. Patients treated with alendronate for 1 year had significantly greater improvement in BMD at spine. The mean BMD at baseline was 0.373 vs

0.773 ($p < 0.005$) and at hip 0.665 vs 0.643 at baseline ($p < 0.005$). Patients who completed two years had similar values of BMD as the year before, the mean BMD was 0.745 at spine and 0.646 at hip.

Conclusion Patients treated with alendronate for one year had significantly greater improvement in BMD at both the spine and hip.

AB0157 PARANEOPLASIC HYPERCALCEMIA COMPLICATING A B CELL NON-HODGKIN LYMPHOMA (NHL)

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Background Hypercalcemia is an unfrequent manifestation of B cell NHL. We describe a case report of hypercalcemia secondary to PTH-rp production, inaugurating a B-cell NHL.

Objectives A 77 year old woman was admitted with dorsalgia. Physical examination was negative except neuropsychological hyperexcitability.

Biological data revealed an increased calcemia (4.2 mmol/l) with decreased phosphoremia (0.45 mmol/l) suggesting a hyperparathyroidism. However, PTH(RIA) was low (3.5 pg/ml, N = 11.0–62.0) and 1.25(OH)2D3 level was in the normal range (40 yg/l, N = 15–80). PTH-rp was moderately increased (2.1 ymol/l, N < 1.5). Bone marrow aspiration was normal. No sign for osteolysis was present on bone X-ray, CT scan and MRI. The abdominal CT scan and abdominal MRI revealed a retroperitoneal mass. A needle biopsy was diagnostic for NHL B type. LDH were elevated to 3290U/l ($n < 470$). Other lymphoid tissue involvement was limited to the spleen. IV farnidronate was successfully administered for treatment of hypercalcemia.

Methods

Results Malignant hypercalcemia occurs in 14p.cent of leukaemia and lymphoma. Among NHL, T cell lymphoma positive for HTLV-1, are more frequently associated with hypercalcemia mediated by production of 1–25(OH)2D3 or lymphotoxin/OAF. Less than 3p.cent of B cell NHL are associated with a paraneoplastic hypercalcemia. Two hypercalcemic mediators have been characterised: PTH-rp and/or OAF

Conclusion Humoral hypercalcemia mediated by PTH-rp is a rare complication of B cell-NHL. Hypophosphatemia with a decreased PTH plasma level must alert for this mechanism.

REFERENCES

- 1 Orsel P. Hypercalcémie des affections malignes, ed. Masson, 1996
- 2 Daroszewska A, Bucknall RC, Chu P, Fraser WD. Severe hypercalcemia in B-cell Lymphoma: combined effects of PTH-rp, IL-6 and TNF. *Postgrad Med J*. 1999
- 3 Hanihara T, Takahashi T. PTH-rp associated Hypercalcemia in probable intravascular lymphoma of B-cell type. *Am J Hematol*. 1996

OP0011 CONSTRUCTION OF A PHYSICAL MAP AND IDENTIFICATION OF CANDIDATE GENES FOR FAMILIAL CHONDROCALCINOSIS AT CHROMOSOME 5P15

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Background A gene for familial chondrocalcinosis was previously mapped to a locus (CCAL2) on chromosome 5p.¹ The purpose of the study was to identify this gene and investigate its role in

the pathogenesis of calcium pyrophosphate arthropathy and osteoarthritis.

Objectives

Methods A combination of physical cloning and candidate gene approach were employed to define CCAL2. Novel expressed sequence tags (ESTs) with expression in cartilage and which mapped to the critical region were identified from EST databases of GenBank. PCR generated DNA fragments from ESTs were radiolabelled using radioactive phosphorus and used as probes in Southern blot hybridization of high density plasmid artificial chromosome (PAC) filters. PACs were identified following autoradiography of the hybridisation membranes and the selected PACs were supplied by the UK HGMP resource centre in Cambridge. The Online Mendelian Inheritance in Man OMIM cytogenetic map was used to identify possible candidate genes within or near the critical region.

Results Six novel ESTs with high cartilage expression, identified 55 PACs following Southern blot hybridization. End sequencing of the PACs allowed the construction of a contig containing 25 PACs across the critical region. Two candidate genes were identified from OMIM. The first gene TRIO codes for a transmembrane multidomain protein which promotes the exchange of GDP for GTP in the extracellular matrix. An abnormality in this pathway is likely to produce an increase in extracellular triphosphate, which has a key role in inorganic pyrophosphate metabolism. The second gene ANK has only recently been mapped to the same location and it is responsible for articular calcification with associated arthritis in mice.

Conclusion The CCAL2 region has been physically mapped and two strong candidate genes are being screened for possible disease causing mutations. This gene should provide a greater understanding of pyrophosphate metabolism and of osteoarthritis with which there is a common association.

REFERENCE

- 1 Hughes AE, McGibbon D, Woodward E, Dixey J, Doherty M. *Hum Mol Genet.* 1995;4:1225–8

OP0115 POLYMORPHISM AT THE TYPE I COLLAGEN (COLIA1) AND RELATIVE RISK OF OSTEOPOROSIS AND VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN

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Background Twin and family studies have demonstrated that an important degree of the population variance in bone mineral density (BMD) is attributable to genetic factors.

Objectives A polymorphism in the collagen type I alpha 1 (COLIA1) gene has recently been associated with low bone mass and fracture incidence.

Methods We analysed the relationship between COLIA1 gene polymorphism, lumbar spine and hip BMD, T-score and fracture incidence in a population of 319 postmenopausal women classified by WHO standards: 98 non-osteoporotic women (NOPW) (57.4 ± 6.2 yrs), 146 osteoporotic women without fracture (OPW without fracture: OPWnF) (60.0 ± 5.2) and 75 osteoporotic women with fracture (OPW with fracture: OPWwF) (61.2 ± 6.3 yrs). The COLIA1 genotype was assessed by polymerase chain reaction and Bal I endonuclease digestion. Genotype

frequencies for the total group were 49.2% "SS" homozygotes, 39.5% "Ss" heterozygotes and 11.3% "ss" homozygotes.

Results We found significant differences in the percentage of homozygous "ss" between NOPW and OPW (6.1% and 13.6% respectively). However, the incidence of genotype "ss" in OPWnF was 6.2% and 28% in OPWwF. We observed no associations between the COLIA1 genotype and lumbar and hip BMD. However, the lumbar spine T-scores were lower in the "ss" group than in the "Ss" and "ss" group. The incidence of fractures (64 vertebral and 11 colles) varied significantly by genotype: "SS" 21.7%; "Ss" 15.9%; and "ss" 58.3% (chi-square = 15.43; $p < 0.0001$); this resulted in a fracture odds ratio of 5.96 (95% confidence interval 2.26–15.69). Logistic regression analysis of fracture prevalence showed that for prevalent fractures, the women with "ss" group had 4.17 times risk of the woman "SS" + "Ss" groups. When prevalence was adjusted for BMD and T-scores, the respective fracture risk was 2.6 and 2.94 for the "ss" group versus the other genotypes (SS+Ss).

Conclusion A slight association was found between lumbar T-score and gene COLIA1 polymorphism. Expression of the "ss" allele seems to be related with a higher incidence of fracture in postmenopausal women and was independent of bone mineral density.

SAT0099 SOFT TISSUE RHEUMATISM IN IRAQI DIABETIC PATIENTS

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Objectives To study the prevalence of soft tissue rheumatism in Iraqi diabetic patients (both IDDM and NIDDM) and to evaluate association between these sequelae and the duration of the disease.

Methods Limited joint mobility (LJM), Dupuytren's Contracture (DC), flexor tenosynovitis (FTS), frozen shoulder (FS) and carpal tunnel syndrome (CTS) were assessed in 100 Iraqi diabetics (50 insulin dependent, 50 non insulin dependent DM) and (50) non-diabetic control matched for age and sex, according to clinical examination (signs and symptoms) and electrophysiological study.

Results Prevalence of LJM, in IDDM vs. NIDDM was (56% vs. 36%), FTS (20% vs. 38%), DC(20% vs 16%), FS(22% vs 40%) and CTS(26% vs 16%).

There was significant statistical difference ($p < 0.05$) between IDDM and NIDDM, regarding LJM, FS, and FTS, the first was higher in IDDM and the last two were higher in NIDDM, while there was no significant and statistical difference regarding CTS and DC.

Conclusion Soft tissue Rheumatism occurs more frequently in both IDDM and NIDDM than in control ($p < 0.05$). Their occurrence appeared to be directly related to disease duration regarding LJM, DC and CTS. The most common sequelae in IDDM was LJM while FS was the most frequent abnormality detected in NIDDM.

Patients with IDDM had been found to be more susceptible to develop multiple rheumatic sequelae than patients with NIDDM($p < 0.05$).