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Correspondence and Short Communications

Comments on published articles, short communications of a preliminary nature, case reports, technical notes and the like are accepted under this heading. The articles should be short and concise and contain a minimum of figures, tables and references.

ONCOGENOUS OSTEOMALACIA—REPORT OF A CASE

Oncogenous osteomalacia is an unusual clinical syndrome characterized by a solitary or focal soft tissue and/or bone tumor producing osteomalacia (1) and manifested by bone pains, pathologic fractures, marked hypophosphatemia, hyperphosphaturia, normal to low level of serum calcium, normal levels of parathyroid hormone and elevated serum alkaline phosphatase (2, 3). Serum 1,25-dihydroxyvitamin D_3 was found to be low in nearly all cases (4). Diffuse osteoporosis and/or Loozer's zones may be seen in all bones. The tumors associated with oncogenous osteomalacia are usually benign and characterized by the predominance of giant cells and spindle cells (87%) and high degree of vascularity (80%) (1, 5). Complete excision of tumors results in cure in the majority of patients (6).

Case report. A 46-year-old white man was admitted to Dokuz Eylul University Hospital for increasing pains localized to right hip joint, right femur, sternum, and ribs and progressive weakness causing marked difficulty in walking. He was first examined in another hospital in June 1989 because of similar pains with 3 years' duration. x-Rays of the right femur then showed lytic bone lesions in the right intertrochanteric area. CT of pelvis revealed a tumor mass in the collum of right femur eroding the cortex of the bone and invading into the surrounding soft tissues. The patient underwent two curettages of this lesion and bone grafting in June and September 1989. Histopathologic examination showed osteochondroblastoma. Physical examination on admission to our hospital revealed marked limitation of movement in the right hip joint, tenderness in this joint, sternum and chest wall. His blood chemistry profile was within normal limits except for elevated alkaline phosphatase 273 U/L (normal: 35–123), decrease in inorganic phosphorus 11 mg/l (normal: 25–48). His serum calcium was normal, 101 mg/l (normal: 88–111). x-Rays of spine, pelvis and long bones revealed diffuse osteoporosis and a lytic lesion in the right intertrochanteric area. MRI of pelvis and right femur showed a tumor mass in the right intertrochanteric area with cortical and medullary damage and protrusion into the surrounding soft tissues (Fig. 1). Radionuclide bone scanning showed increased uptake in vertebrae, ribs and pelvis. A posterior segment of the right 7th rib, showing increased radionuclide uptake, was biopsied and histopathology revealed callus formation, vascular proliferation and osteomalacia but no atypical cells (Fig. 2). Review of slides prepared from paraffin blocks of the tumor in the right intertrochanteric area in June 1989 showed tumor tissue composed of round, ovaloid and/or spindle shape cells and prominent vascularity with reticular stroma. Osteoclast-like giant cells were also identified in the areas of tumor tissue. Unmineralized osteoid tissue which is typically seen in osteomalacia was found around the lesion. Biochemical studies on 24-h urine demonstrated glycosuria, proteinuria and hyperphosphaturia without aminoaciduria. Blood chemistry showed decreased inorganic phosphorus of 16 mg/l (normal: 25–48). His fasting blood glucose was 980 mg/l (normal: 700–1100), blood pH 7.42 and blood bicarbonate 27 mmol/l (normal: 23–26). The serum parathyroid hormone level was normal. Parathyroid scintigraphy failed to demonstrate adenoma or hyperplasia. Serum 25-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol levels could not be determined. The diagnosis of oncogenous osteomalacia was established and in February 1992 the tumor in the one third proximal part of right femur was surgically removed and replaced by an artificial hip joint. Following the surgery his symptoms cleared up in about 2 weeks. The blood inorganic phosphorus returned to normal level one month later with the disappearance of hyperphosphaturia in the urine. His last visit was in December 1993 and he has been doing very well without any evidence of disease.

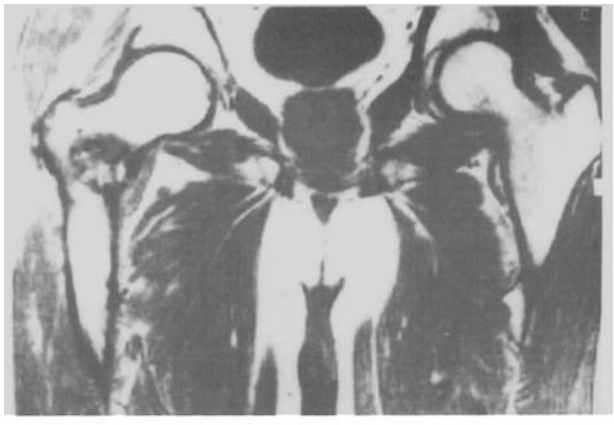

Fig. 1. Demonstrating a tumor mass localized in the right intertrochanteric area producing cortical and medullary damage with protrusion into the surrounding soft tissues by MRI.

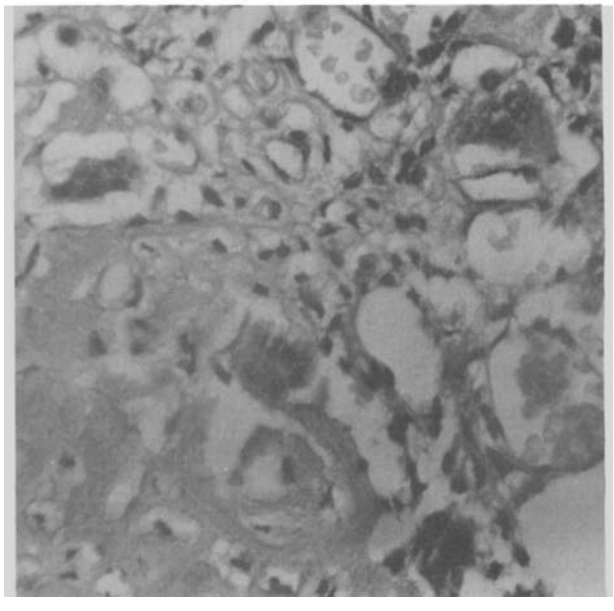

Fig. 2. Biopsy from a rib showing osteoid tissue with thin walled-large dilated vessels filled with red blood cells, small capillary vessels and osteoclast-like multinucleated giant cells (HE × 400).

Discussion. In the reported case the diagnosis of oncogenous osteomalacia was made by detection of hypophosphatemia, and hyperphosphaturia with normal levels of serum calcium and parathyroid hormone and demonstration of vascular proliferation and osteomalacia in the resected rib in addition to the findings of

spindle shape and osteoclast-like giant cells and prominent vascularity in the excised tumor by histopathologic examination and diffuse osteoporosis by x-rays. Disappearance of hypophosphatemia, hyperphosphaturia, glycosuria, proteinuria and the dramatic clearance of his symptoms following removal of the tumor were also con-firmatory evidences for the diagnosis of oncogenous osteomalacia. Recognition and removal of the tumor in patients with oncogenous osteomalacia restores the severe and total disability (7). In conclusion, oncogenous osteomalacia should be suspected in any patient who presents with metabolic bone disease associated with hypophosphatemia and inappropriate phosphaturia, in combination with a benign mesenchymal soft tissue or bone tumor. The possibility of metastatic malignant disease should be ruled out by biopsies of the bones guided by bone scan or x-ray examinations.

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IS GASTRIC CANCER HETEROGENEITY THE CLUE TO HLA-DR ASSOCIATED SUSCEPTIBILITY?

Worldwide, gastric cancer remains a leading cause of cancer death (1). Despite recent advances (2), the role of genetic and immune factors for the development of gastric cancer remains unclear. A genetic component was suggested when increased frequency of blood group A was found in patients with gastric cancer (3). Subsequent studies have confirmed that heredity may be important for the development of this malignancy (4–7). The genetic regulation of immune phenomena mainly occurs within MHC, and HLA-DR antigens play a crucial part in initiating the specific immune response. It has therefore been suggested that phenotypic HLA-DR differences may be associated with different risks of developing neoplastic diseases. However, in three reported population studies on HLA-DR and gastric cancer no constant relation was found (8–10), and the same concerned earlier investigations of HLA class I antigens (11–13). One reason for the conflicting results may be gastric cancer heterogeneity (1, 2, 14, 15). These facts prompted us to investigate the association of HLA-DR antigens with gastric cancer taking into consideration its types according to the Järvi-Lauren classification, tumour grade, stage, and topographical classification.

Material and Methods. Forty-six consecutive, unrelated patients (35 males and 11 females) of Polish ancestry with resectable and histologically proven gastric carcinoma have been prospectively tested since 1989 and typed for 10 HLA-DR specificies (DR1, DR2, DR3, DR4, DR5, DRw6, DR7, DRw8, DR9, DRw10) by a standard microlymphocytotoxicity technique (16, 17). Lymphocytes were isolated by gradient centrifugation and T and B cell separation was performed with AET-treated sheep erythrocytes. The serotyping trays were 'Lymphotype-DR' (Biotest Diagnostics). The controls consisted of 389 Polish individuals. Antigen frequencies were calculated in the control group, the total cancer group and in subgroups of patients categorized according to the Järvi-Lauren classification (14) (24 patients with intestinal type (Int), 14 with diffuse type (Dif) and 32 with intestinal and mixed types (Int + M)), WHO histological grading (15) (26 patients with adenocarcinomas with high or moderate grade of differentiation (H + M) and 20 with poorly differentiated adenocarcinoma or undifferentiated carcinoma (P + U)), TNM-AJC classification of tumour extension—T (15) (12 patients with T1 or T2, 43 with T2 or T3 or T4, 22 with T1 or T2 or T3, and 24 with T4) and topographical classification (15 patients with the tumour located in the cardiac region—Car, 27 in the fundus or body—Fun + Cor, 21 in the pyloric region—Pyl). The antigen frequencies in the groups were compared using the χ^2 test with Yates' correction. The strength of association was estimated by calculating the relative risk (RR).

Results. HLA-DR typing results in the 46 patients with gastric cancer are shown in Table 1. Only the HLA-DR5 frequency was

Table 1

HLA-DR antigens distribution among 46 gastric cancer patients and 389 controls

HLA specificity	Frequency (%) patients	Frequency (%) controls	χ^2	p-value
DR1	28.3	20.3	1.12	N.S.
DR2	23.9	25.2	<0.01	N.S.
DR3	19.6	22.4	0.06	N.S.
DR4	17.4	19.3	0.01	N.S.
DR5*	34.8	20.1	4.44	< 0.05
DRw6	13.0	14.9	0.01	N.S.
DR7	21.7	26.5	0.27	N.S.
DRw8	4.3	5.7	<0.01	N.S.
DR9	4.3	3.6	0.03	N.S.
DRw10	4.3	3.3	<0.01	N.S.
DRx	28.3	38.6	1.45	N.S.

* RR = 2.13
DRx—unidentified antigens or homozygotes