2) ITAI-ITAI (pain-painful) Disease

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This disease affects mainly women above 40 years of age and occurs in a small area along the Jinzu River. The most common complaints consist of bone and joint pain and bone lesions which are similar to senile osteomalacia have been reported as a major pathology. However, it has been known that most of them had proteinuria and glycosuria.

We studied renal aspects of this disease in 4 established cases. The major abnormality was generalized tubular defects composed of proteinuria, non-hyperglycemic glycosuria, non-specific aminoaciduria, hypophosphatemia with low tubular reabsorption of phosphate and hyperchloremic acidosis. Decreased clearances of PAH and thio-sulfate, highly impaired PSP-excretion, and nonfunctioning curves in renogram with normal blood NPN were thought to indicate the existence of decreased tubular secretion. Kidney biopsy in 3 cases revealed essentially normal glomeruli, dilated tubules with flat and degenerative tubular cells and diffuse interstitial fibrosis.

These findings are entirely compatible with Fanconi's syndrome and screening tests (including urinalysis) revealed high incidence of proteinuria and glycosuria in the endemic area. So we believe that the bone changes which were thought to be the main abnormality of the disease, are secondary to the tubular dysfunction.

Endemic outbreaks without hereditary factors suggest the possibility of exogenous intoxication, especially heavy metals, as the etiology of this disease. Among the metals, Cd is the most suspected, because it was reported that soil in the affected area was contaminated with Cd, Pb and Zn and that patients excreted a large amount of Cd in urine as compared to rather low urinary Pb and Zn. However, poor nutrition, Ca-depletion due to multiple conceptions and parturitions and/or endocrine disturbances might have played secondary roles in the development of bone lesions in middle-aged women.