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Case Report

Primary (Autoimmune?) Parathyroiditis

M. Van de Casseye and W. Gepts
Department of Pathology, Brugmann University Hospital, Brussels

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Summary. A case of idiopathic hypoparathyroidism associated with Paget's disease in an eightyfive-year-old man is reported. Pathological and biological features suggest the possibility of an autoimmune aetiology. The association of idiopathic hypoparathyroidism and Paget's disease is probably fortuitous.

Introduction

Hypoparathyroidism in the adult without prior thyroidal surgery is a rare disease. The literature on its pathological aspects is scarce and its possible aetiologies are poorly defined.

We are reporting here a case of idiopathic hypoparathyroidism in an eighty-five year old male suffering from Paget's disease. On pathological examination of the parathyroids a chronic inflammation was noted, which together with immunological findings suggested the possibility of an autoimmune aetiology.

Clinical Observation

An eighty-five year old patient was admitted to the hospital following an accidental fall. He was found to be disoriented in time and space and displayed strong generalized convulsions. It was learned that similar convulsions had appeared at irregular intervals during the preceding months.

Physical examination revealed a slender male with frontal alopecia and bilateral cataracts. Partial temporal epilepsy was made as a preliminary diagnosis. However laboratory tests revealed a calcemia at 5 mg/100 ml, a phosphoremia of 6 mg/100 ml and a magnesemia at 1.1 mg/ml, alkaline phosphatases were 29 U (King-Armstrong). The γ globulins were high: 20.9% for 7 g/100 ml of total proteins.

No parathormone could be detected in the serum with a sensitive radioimmunoassay method. Antibodies against thyroid or parathyroid tissues were not found in the serum.

An electroencephalogram proved to be normal but an X-ray of the skull showed a right-sided frontoparietal fracture, that was probably a consequence of the accidental fall. X-ray of the pelvis suggested Paget's disease which was confirmed by iliac crest biopsy. Other parts of the skeleton presented no radiological discernible anomalies.

The evolution of the patient's condition was characterized by progressive renal insufficiency caused by prostatic hypertrophy. A staphylococcus aureus antibiotic resistant urinary infection complicated the situation. The patient died with symptoms of bronchopneumonia and septicemia.

Pathology

At Autopsy. The parathyroids were difficult to find. Several small tissue fragments were removed from the normal anatomical location of these glands. The thyroid was moderately increased in volume and contained a colloidal cyst.

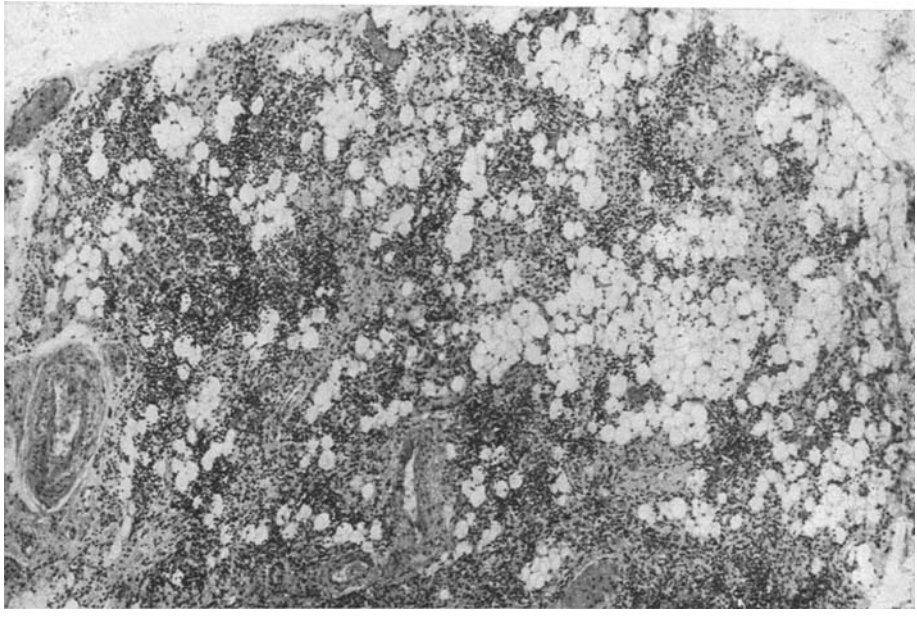

Fig. 1. Parathyroid gland showing a diffuse lymphocytic infiltration, with atrophy of the endocrine cells and severe lipomatosis. Hematoxylin-eosin-saffron. Magnification: 125

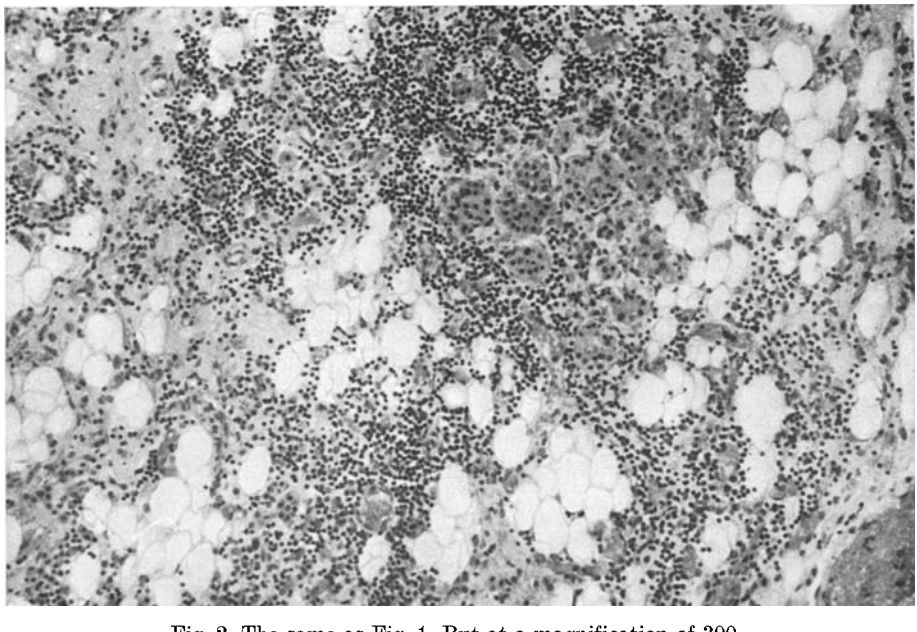

Fig. 2. The same as Fig. 1. But at a magnification of 300

Other major findings were: bilateral lesions of bronchopneumonia with an abcess in the right upper lobe; a scar from a myocardial infarct in the posterior wall of the left ventricule; chronic cholecystitis with lithiases; severe pyelonephritis with necrotic papillitis; marked adenomatous hypertrophy of the prostate; hemorragic cystitis.

Histopathology. Parathyroids were identified in two of the samples taken. They contained normal proportions of principal cells and oxyphilic cells. The cells in certain areas formed small colloid containing vesicles. The epithelial cells were unequally distributed in an important adipose stroma. But, the most interesting finding was the presence in the interstitium of a very dense, diffuse, inflammatory infiltration, composed mainly of lymphocytes and plasmatocytes (Fig. 1). This infiltration was limited to the parathyroids, there being no degenerative lesions of the parathyroid cells itself (Fig. 2). No inflammatory lesion or atrophy was found in any of the other endocrine glands examined. In the other organs the histologic examination confirmed the macroscopic pathological findings.

Discussion

Excluding hypoparathyroidism as a consequence of thyroidal surgery and pseudohypoparathyroidism various aetiologies have been proposed for the so-called idiopathic hypoparathyroidism.

Transitory hypoparathyroidism has been reported in the newborns, prematures and in infants born to hyperparathyroid mothers (Balsan, 1968; Ertel, 1969; Orme, 1971). It has been explained by an inhibitory effect of maternal hypercalcemia on the development of the foetal parathyroid tissue.

A familial incidence in cases occuring during the first year of life has been linked with a recessive hereditary factor (Peden, 1960). Sporadic cases have been proved to result from an agenesis of the parathyroids (Taitz, 1966; Lobdell, 1959; Gilmour, 1941). Other aetiologies have been proposed for cases occuring after the first year, but many among them lack supportive evidence or were at best applicable only to isolated incidences: anomaly of magnesium metabolism (Massry, 1970; Ertel, 1969), cystic fibrosis (Morse, 1961), hemosiderosis due to thalassemia major (Gabrielle, 1971).

In the adult and infants, few cases of primary hypoparathyroidism have been documented from the pathological point of view. However review papers on the subject have been published by Steinberg (1952), Bronsky (1958), Kopin (1960), Taitz (1966). The suggested aetiologies are numerous: hemorrhages, rheumatoid lesions, cysts, malignant invasions, bacterial embolism, tuberculosis, syphilis, typhoid fever, and viral infection (Drake, 1939). None of these hypothesis can be applied in our case.

In both infants and adults, idiopathic hypoparathyroidism associated with thyroiditis and/or Addison's syndrome, have been recorded. This association suggests the possibility of an autoimmune aetiology. Other arguments support this hypothesis. Antibodies against parathyroid tissue were found in 38% of cases of primary hypoparathyroidism, whereas they are present in only 6% of a normal control population (Kenny, 1964; Irvine, 1969; Hung, 1963; Spinner, 1969). Moulias (1971) studied cellular immunity in eight patients with idiopathic

hypoparathyroidism with the aid of the leucocyte migration inhibition test. The result was positive in 5 cases. Lymphocytic parathyroiditis was induced experimentally in dogs by isoimmunisation against parathyroid tissue (Lupulescu, 1968).

In our case, the lymphocytic infiltration of the parathyroids with atrophy of the endocrine cells supports an autoimmune aetiology. The significance of this finding though, is somewhat weakened by the observations of Reiner (1962) and of Seemann (1967). These authors performed a systematic study of the parathyroids in a large number of autopsies. Reiner found lymphocytic and plasma cell infiltration in 10% of 144 patients between the ages of 35 to 77. In Seemann's material inflammatory infiltration, predominantly lymphocytic, was discovered in 16% of 225 cases between birth and 90 years of age. In Reiner's cases the infiltration was mild or moderate, whereas Seemann classified it as mild (15 cases), moderate (18 cases) or severe (5 cases). Only in one case did Seemann consider the histologic picture to be evocative for immune parathyroiditis. Clinical or biological indications of hypoparathyroidism had not been recorded in this case, but they had not been looked for. In a personal study of the parathyroids of 55 patients between the ages of 23 and 88, we found a moderate infiltrate in three only, and not the slightest infiltrate in the others. Other positive arguments in favour of an autoimmune origin of our case, are the positive leucocyte migration inhibition test and a raised serum γ globulin to 20.9% for 7 g% of total proteins.

It is true that we were unable to demonstrate circulating antibodies against parathyroid tissue, but this does not rule out an immune origin. In his series of 74 cases, Blizzard (1966) could demonstrate antibodies only in 38% of them Spinner (1969) found antibodies in 11% of his 70 cases. Furthermore it is a well established fact that autoimmune reactions in organs are effected principally by immunocompetent lymphoid cells and are not necessarily associated with the presence of circulating antibodies.

Characteristic bone lesions have not been described in true hypoparathyroidism, in contrast to pseudohypoparathyroidism. Does the association of hypoparathyroidism on Paget's disease, observed in our case, have a physiopathological implication or is it purely coincidental? In literature, we found only one other example of such an association (Pitman, 1969), but in that case hypoparathyroidism was secondary to thyroidectomy. Taking into account the high frequency of Paget's disease (Collins, 1956; Schmorl, 1932) in patients over 40 years of age, i.e. 3%, we feel that in our case the association is probably due to coincidence.

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M. Van de Casseye
Department of Pathology
Brugmann University
Hospital of Brussels
Brussel (Belgien)