Hyperplastic parathyroiditis—a new autoimmune disease?

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SUMMARY A case of parathyroiditis with epithelial hyperplasia is reported in which the histological features suggest an autoimmune process analogous to Hashimoto's disease.

Microscopic evidence of autoimmune thyroiditis is frequently found at necropsy in apparently euthyroid individuals.^{1,2} The abnormalities in these glands range from mild focal chronic thyroiditis to those of classical Hashimoto's disease.³ Focal lymphocytic infiltration of parathyroid glands has also been found at necropsy in up to 10% of patients assumed to be euparathyroid.⁴ In the few reported necropsy cases of primary hypoparathyroidism in which parathyroid glands could be positively identified, the histological appearances were of parenchymal atrophy with mild focal lymphocytic infiltration,^{5,6} reminiscent of the diffuse, atrophic variant of autoimmune thyroiditis found in primary myxoedema.⁷ A histological equivalent of Hashimoto's disease in which epithelial hyperplasia accompanies thyroiditis⁸ has not been reported to date in the parathyroid glands. In this paper we report the first such case.

Case report

The patient was a 48-year-old woman who died accidentally in a house fire in 1979. She had chronic bronchitis and had been attended by her general practitioner since she developed a left hemiplegia in 1975. She had no other medical complaints and lived with her sister who enjoyed good health. There was no family history of autoimmune disease.

NECROPSY FINDINGS

There were extensive burns which accounted for her death. A large apoplectic cyst occupied most of the right cerebral hemisphere. The only other abnormality noted was global myocardial fibrosis. The thyroid, pituitary and adrenal glands were normal on naked-eye examination. The parathyroid glands

were not noted to be enlarged when removed along with some perithyroid lymph nodes.

HISTOLOGY OF PARATHYROID GLANDS

When the parathyroid glands were identified histologically, three were increased in size (approximately 2–3 times normal area). Their histological appearance, illustrated in Figs 1–4, is reminiscent of Hashimoto's thyroiditis—namely, a heavy focal infiltrate of lymphocytes and plasma cells with several lymphoid follicles containing germinal centres, increased amount of parathyroid parenchyma composed of chief cells and oxyphil cells amid widespread focal fibrosis with associated parenchymal cell loss. The fourth parathyroid gland was normal in size and in its centre there was a stellate infiltrate of lymphocytes and plasma cells associated with fine fibrosis and parenchymal cell loss. There was minimal fatty replacement of glandular tissue in all of the glands. The thyroid gland was histologically normal, and a wedge of bone from the iliac crest showed no evidence of disease. No other tissues were examined histologically since the necropsy was carried out for medicolegal purposes.

SEROLOGICAL STUDIES

In view of the histological evidence of autoimmune parathyroiditis, circulating antiparathyroid antibodies were sought by indirect immunofluorescence using undiluted patient's serum and unfixed frozen sections of normal and neoplastic parathyroid tissue. Antibody was not detected. Using standard serological techniques the patient's serum was subsequently screened for other antibodies (including antithyroglobulin, adrenal cortex, salivary duct, mitochondrial, and smooth muscle antibodies) and rheumatoid factor, all with negative results.

Discussion

The microscopic features of this case closely resem-

Fig. 1 Low magnification of an enlarged parathyroid showing 3 lymphoid follicles with pale staining germinal centres. There is also extensive parenchymal replacement by fibrous tissue in the lower half of this field. Haematoxylin and eosin $\times 90$.

Fig. 2 Low magnification of another enlarged gland showing prominent bands of fibrous tissue intersecting islands of parathyroid parenchyma which consists of chief cells and oxyphil cells. A single lymphoid follicle is present at upper right. Haematoxylin and eosin $\times 90$.

Fig. 3 High power magnification of Fig. 2 showing, in greater detail, the chief and oxyphil cells intersected by fibrous tissue bands. The inflammatory component consists of plasma cells and lymphocytes. Haematoxylin and eosin $\times 565$.

Fig. 4 Low magnification of the small parathyroid showing unremarkable parenchyma and fat with focal aggregates of lymphocytes and, to the left of centre, an area of stellate fibrosis. Haematoxylin and eosin $\times 90$.

ble the thyroid lesions in Hashimoto's disease (lymphoid and epithelial hyperplasia and fibrosis⁸) and are suggestive of organ-specific autoimmune parathyroiditis. This impression is not incompatible with normal parathyroid function since the abundant parathyroid tissue found in three of the glands could

well have been functional. Indeed, in Hashimoto's disease up to 50% of patients have normal thyroid function.⁹

Autoimmune destruction of the parathyroid glands is thought to account for most cases of primary acquired (idiopathic) hypoparathyroidism,^{6,10}

although there have been few necropsy studies of the glands. In some cases, the minute, atrophic glands have not been positively identified,¹¹ in others they were completely replaced by fat.¹² The histological findings in two studies in which the glands were identified^{5,6} consisted of focal infiltration by lymphocytes and plasma cells with glandular atrophy and fatty replacement of parenchymal tissue. Lymphocytic infiltration of varying severity has been described in up to 10% of parathyroids examined during routine necropsy of patients with normal gland function,⁴ suggesting a parathyroid equivalent of focal chronic thyroiditis.

Further evidence of an autoimmune process is the finding by Blizzard *et al*¹³ of antibody to parathyroid tissue in 28 of 74 cases (38%) of idiopathic hypoparathyroidism. These workers observed that 18 of the 74 cases had Addison's disease, seven had pernicious anaemia, and six had thyroid disease, all members of the group of so-called "organ-specific autoimmune diseases." Involvement of other organs is common in primary hypoparathyroidism, which itself occurs commonly in Addison's disease.⁴ Our negative serological findings are similar to those of others⁶ who have also failed to confirm Blizzard's original observations in cases of primary hypoparathyroidism.

Primary hypoparathyroidism is usually diagnosed in childhood or adolescence, but can present at any age.¹⁰ The patient described by Van de Casseye and Gepts⁵ presented with hypoparathyroidism at 85 years of age. It is conceivable that our patient might subsequently have developed clinical hypoparathyroidism had she survived.

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