Letters to the Editors

Sir, Pestell, Best, and Alford's (1990) review of lymphocytic hypophysitis makes several valid points regarding this rare disorder. However, the authors have not mentioned all the reported cases.

There have been at least 30 cases reported in the literature, as well as the two presented by the authors. Two recent cases have been seen in the Royal Adelaide Hospital (unpublished).

Cases from Baskin et al. (1982), Sobrinho-Simoes et al. (1985), Madsen et al. (1985), Wild and Kepley (1986), Okamoto et al. (1986), Gal et al. (1986), McGrail et al. (1987), Vaneste and Kamphorst (1987), Levine et al. (1988), and the three cases of Cosman et al. (1989) were not mentioned by the authors.

Whilst there has been no report of systemic leucocytosis in previous cases, neutrophil infiltration of the pituitary has been seen in five histological sections (Asa et al., 1981; Baskin et al., 1982; Cebelin et al., 1981; Guay et al., 1987; Portocarrero et al., 1981) in addition to the authors'.

Asa et al. (1981) reported two cases (not three); the first noted some improvement in tumour size with bromocriptine. In addition, the case reported by Vaneste and Kamphorst (1987) had resolution of galactorrhoea without change in tumour size, following the use of bromocriptine. The suggestion that bromocriptine is associated with some reduction in lactotroph hyperplasia in this context has not been made before.

Prolactin levels are often abnormal, but are more frequently inappropriately low (10 of 28 cases), being mildly elevated in only eight cases. In three cases, prolactin levels have been normal, and in six cases, the level of prolactin was not measured.

Intrasellar pathology with suprasellar extension seen on CT scan is seen in 70% of cases. There have been no cases described apart from the authors' first case, with ectopic pituitary tissue. It is uncertain from the description given what in fact the contents of the pituitary fossa were. An empty fossa may be an explanation, if partial pituitary necrosis had occurred.

The time course of the authors' second case is the longest described. The only other male patient to be described (Guay et al., 1987) had symptoms for 12 months and the longest previously documented duration of symptoms has been 3 years' amenorrhoea in a 31-year-old woman (Wild & Kepley, 1986).

Whilst the authors suggest that adrenal insufficiency may be an early mode of presentation, it is possible that adrenal insufficiency has gone undetected in some patients, and a (frequently) fatal adrenal crisis has been its first manifestation, even several years after the onset of symptoms (Hume & Roberts, 1967; Guay et al., 1987).

Symptoms of hypoadrenalinism have been present in all cases (unfortunately often in retrospect). At autopsy adrenal atrophy was seen in all but one case (Egloff et al., 1969).

Adrenalin insufficiency was present in 80% of cases studied ante-mortem. There is no documentation of an assessment of adrenal reserve in the case mentioned.

Antibodies directed against thyroid, adrenal, pituitary or gastric parietal cells have been found in 30% of patients studied. Lymphocytic infiltration of the thyroid has been seen at autopsy, but antimicrosomal antibodies are not commonly seen.

Insulin-dependent diabetes has not previously been a described association of lymphocytic hypophysitis. There appears to be no strong evidence for an immunogenetic link between lymphocytic hypophysitis and either autoimmune thyroid disease or insulin-dependent diabetes.

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References


Levine, S.N., Benz, E.C., Fowler, M.R., Shroyer, J.V. & Mirakh-


Sirs, We thank Dr Stolz for his letter noting the review by Cosman et al. (1989), and references within. These reports increase the number of descriptions but add little to explain the spectrum of this disease.

It is important to correct some of the erroneous statements in his letter. The reference to Baskin et al. (1982) was included by us. The description by Asa et al. (1981) includes three patients (p. 170). Neutrophil infiltration is not a feature of the histological sections quoted by Dr Stolz, and his comments are therefore misleading. His error may relate to a misunderstanding of the text. For example, Guay et al. (1987) describes a 'polymorphous population of chronic inflammatory cells, mature lymphocytes, plasma cells, cosinophils'.

Dr Stolz observes, as we stated, that in lymphocytic hypophysis, adrenal insufficiency occurs commonly, contrast-enhancing masses may be seen on CT scan, and prolactin levels vary. The diagnosis of adrenal insufficiency in the context of hypopituitarism in our second case we based on the clinical appearance described in our text and was confirmed by the dramatic response of the patient's marked postural hypotension to cortisone replacement within 24 h, and therefore further testing was not justified.

Dr Stolz's proposal that the tumour of our first patient arose from within the sella turcica is untenable. The conclusion of ectopic origin of the mass, made by a most experienced neurosurgeon, was based upon the presence of an intact diaphragm sella, through which a normal pituitary stalk passed. The diaphragm sella was concave downwards from compression by the extra-sellar mass. Upon removal of the mass, normal appearing pituitary tissue was visualized within the sella turcica.

A link between lymphocytic hypophysis and autoimmune thyroid disease has been suggested by the common association with 'lymphocytic thyroiditis' (7/30 Catel, Cosman et al., 1989). Our evidence for an association with autoimmune thyroid disease and diabetes related to the HLA typing observed in our patients (Petrell et al., 1990).

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**References**


Sirs, We read with interest the paper entitled 'The effect of amiodarone on the control of hyperthyroidism by propylthiouracil' by Rajatnavin et al. (1990).

The treatment of hyperthyroid patients with amiodarone in conjunction with a thionamide is not original (Van Reeth et al., 1987). The data published with oral cholecystographic agents used alone as inhibitors of peripheral T3 generation and 'in-vivo generators of iodine' have demonstrated the risk not only of escape or recurrence of hyperthyroidism but frank exacerbation of the disease (Fuller & Stockigt, 1982) so that combination with a thionamide has been recommended by Larsen (1982). We have data supporting Rajatnavin's assumption that a thionamide may prevent repletion of
thyroid iodine by amiodarone. Two Graves' patients who remained hyperthyroid while on methimazole because of poor compliance were prepared for surgery with amiodarone and methimazole. Patient 1 received 6.4 g amiodarone in 7 days with 80 mg methimazole and patient 2, 5.2 g amiodarone in 4 days with 60 mg methimazole. Intrathyroidal iodine concentrations in the surgical samples were low, 123 and 154 μg/g tissue respectively (mean value for euthyroid subjects in Brussels: 280 μg/g). Nevertheless, the prolonged release of iodine—as demonstrated by urinary iodine measurements (Unger et al., 1990)—even after 3 days administration of a total dose of 3.6 g amiodarone, remains of concern. Indeed, if the thionamide is withdrawn because of serious side-effects, the patient is left with the problem of iodine used alone, and hyperthyroidism may recur. The prolonged release of iodine also precludes the administration of radioiodine. In our patients, urinary iodine was still slightly elevated 3 months after the cessation of amiodarone but radioiodine could be administered (Van Reeth et al., 1987).

The speculation by Rajatanavin et al. that iodine from amiodarone inhibits thyroid secretion, although likely, is based on two studies (Sheldon, 1983; Shian et al., 1985) in which the dose of iodide presumably equivalent to that liberated from amiodarone was extrapolated from chronic administration of amiodarone (Broekhuysen et al., 1969). After acute administration of amiodarone, whether in euthyroid (Contreras et al., 1985; Studer et al., 1979) or hyperthyroid (Unger et al., 1990) patients, the daily release of iodide is much lower.

We agree that iodide release and decreased peripheral T₃ production are beneficial in hyperthyroidism but these properties do not justify the use of amiodarone. Lugol or SSKI remain preferable as iodide providers because of their short half-lives. To inhibit peripheral T₃ generation, dexamethasone is effective and doses of PTU higher than 300 mg daily may be administered. With 600 mg PTU/day, 1200 mg amiodarone daily still reduces T₃ concentration (Unger et al., 1990) but the beneficial effect of amiodarone with 1000-1500 mg PTU remains to be demonstrated.

The main interest of amiodarone is that it is the only 'anti-thyroid' drug with antiarrhythmic properties. Atrial fibrillation is often associated with thyrotoxicosis and may induce thromboembolic events so that prompt reversal to sinus rhythm should be sought. Propranolol (Cooper & Ridgway, 1985) and verapamil (Dahlstrom & Ladeoged, 1987) or diltiazem (Roti et al., 1988) may help to decrease the ventricular rate in atrial fibrillation but only infrequently reverse it to sinus rhythm. In contrast, amiodarone may reverse atrial fibrillation, even when it is refractory or associated with thyrotoxicosis (Litvinenko et al., 1982). We have shown the beneficial effects of amiodarone on both thyroid hormone levels and cardiac rhythm in patients with thyrotoxicosis-associated atrial fibrillation (Cauchie et al., 1988; Unger et al., 1990). In this condition, amiodarone may be preferred to the beta-blockers even when they are not contraindicated.

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References


medical treatment of myocardial infarction', Zurich. Scientific Reports. Sanoft Research Center of Brussels, Belgium.

Sirs, We thank Drs Unger and Van Reeth for providing clinical data to support our thesis that a thionamide in conjunction with amiodarone may prevent repletion of thyroid iodine.

We also agree that amiodarone should not be used as a first-line drug for therapy of hyperthyroidism but may be utilized in situations when rapid amelioration of hyperthyroidism is needed. This is emphasized in the last paragraph of our article.

As to the originality of the treatment of hyperthyroid patients with amiodarone in conjunction with a thionamide, we reported and presented our data in the form of an abstract at the Eighth Asia and Oceanic Congress of Endocrinology in Bangkok in 1986 (Rajatanavin et al., 1986). However, we were unaware of Drs Unger and Van Reeth's paper (Van Reeth et al., 1987) and we regret our failure to cite it in our article.

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References

Sirs, The article by Wu and associates (1989) illustrates how the clinical presentation of diffuse sclerosing papillary carcinoma can be a source of confusion for physicians. An important clinical aspect of this variant of thyroid carcinoma is that the affected patients have measurable titres of antithyroid antibodies in their sera (Chan et al., 1987; Gómez-Morales et al., 1991). This fact, along with the diffuse thyroid enlargement, can lead to a clinical diagnosis of benign disease, particularly autoimmune thyroiditis or multinodular goitre, as occurred in the three patients reported by Wu et al. (1989).

We have studied four patients with this variant of papillary carcinoma (Gómez-Morales et al., 1991), and all but one, who was under steroid treatment, had a positive test for antithyroid antibodies. In one case, the high level of antibodies to thyroid microsomes detected in the serum and the diffuse involvement of the thyroid gland led to a clinical diagnosis of Hashimoto's thyroiditis. This peculiar clinical presentation emphasizes the value of fine-needle aspiration cytology as a diagnostic tool, since in all our patients a correct diagnosis of papillary carcinoma was reached by this method.

Histologically, a major characteristic is the presence of squamous metaplasia (Vickery et al., 1985; Chan et al., 1987). In agreement with previous reports (Chan et al., 1987) the immunohistochemical analysis of thyroglobulin in our four cases showed an irregular distribution of this antigen, positive cells alternating with cells devoid of immunostaining, and was completely absent in areas of squamous metaplasia. As the squamous component is so widespread in diffuse sclerosing papillary carcinoma, it is tempting to suggest that this tumour is of low functional activity. This fact is probably responsible for the low level of thyroglobulin (< 3 ng/ml) detected in one of our patients, after total thyroidectomy, when lymph node metastases developed which were demonstrated by histological study.

These events make diffuse sclerosing papillary carcinoma a peculiar type of thyroid carcinoma which offers some difficulties not only in the clinical diagnosis but also in the follow-up of patients harbouring this variant of thyroid carcinoma.

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References