Int J Legal Med (1999) 112 : 271–274

CASE REPORT

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Inflammation of the cardiac conduction system in a case of hyperthyroidism

Received: 13 July 1998 / Received in revised form: 15 September 1998

Abstract A 37-year-old female showed signs of hyperthyroidism 2 weeks before death after a partial thyroidectomy was carried out 15 years previously. An examination 3 days before death revealed a normal blood cell count, an increased level of thyroidal hormones, sinus tachycardia and a high blood pressure of 170/90 mm Hg. A hyperthyroidism was diagnosed and therapy with carbimazol (2 × 10 mg) was started but 2 days later fever and chill occurred and before death short phases of unconsciousness and dyspnoea. The autopsy findings showed an interstitial inflammation of the AV-node, the His-bundle and its branches which can correlate with typical ECG changes in hyperthyroidism.

Key words Hyperthyroidism · Thyrotoxicosis · Myocarditis · Cardiac conduction system

Introduction

Morphologically unclear deaths of patients with hyperthyroidism are rare but well known (Edston 1996; Herman et al. 1986; Parker and Lawson 1973; Randall 1992; Simon 1976). Thyrotoxicosis can cause sudden death by several mechanisms including cardiac arrhythmia, myocardial infarction, hyperpyrexia, electrolyte disturbances and epileptic seizures (Burch and Wartofsky 1993; Nakano et al. 1987; Woeber 1992).

There are no lesions in the heart which are characteristic for thyrotoxicosis, and necrosis of the myocardium and interstitial myocarditis have been found in only a few cases whereas myocardial glycogen and lipid changes were more abundant (Batsakis 1968; Bhasin et al. 1981; Friedberg 1972; Roskamm and Reindell 1996). However, it is not clear if the thyroid disease caused these alterations or if the changes were merely a non-specific end-result from overwork of the heart. However, typical changes in the electrocardiogram (ECG) are known. First degree A-V block has been frequently reported with an incidence of about 5% of patients without other heart disease (Benker et al. 1974) and Goodall and Rogers (1927) reported a P-R prolongation in 30% of the patients. Sporadic case reports link Graves' disease with a high degree AV-block and syncopes (Archambeaud-Mouveroux et al. 1987; Miller et al. 1980; Muggia et al. 1970). We report a case of hyperthyroidism in which a P-Q prolongation is possibly in causal connection with an interstitial myocarditis of the cardiac conduction system (CCS).

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Case report

A 37-year-old woman complained about unrest, nausea, vomitus and stomach pains 2 weeks before death. A clinical and analytical examination 3 days before death revealed a γ-glutamyl-transferase level of 33 U/l, an erythrocyte sedimentation rate of 72 mm/h, normal red and white blood counts and increased levels of thyroidal hormones (see Table 1). The ECG demonstrated a sinus tachycardia with 120 beats/min and moderate changes of the excitement regression with horizontally lowered ST-distances especially in V3-V6. The blood pressure was 170/90 mm Hg. A chest x-ray revealed a normal size heart with clear lung fields. A hyperthyroidism was diagnosed and a therapy with carbimazol 2 × 10 mg was started. However 2 days later the patient suffered from fever and chill and short phases of unconsciousness and dyspnoea alarmed the relatives and an ambulance was called. The patient was very restless and a psychoactive drug (Triflupromazin 20 mg i.m.) was given. A short time later an acute cardiac arrest occurred and resuscitation attempts failed. The clinician assumed that death was caused by an arrhythmia due to thyrotoxicosis.

Table 1 Comparison of hormone levels in the patient with normal levels

Hormone	Antemortem 3 days	Postmortem 8 h	Reference values (antemortem)
T3	3.2 ng/ml	1.09 ng/ml	0.7– 1.8 ng/ml
T4	18.5 μg/dl	20.5 μg/dl	5 –12 μg/dl
TSH	0.1 μU/ml	–	0.3– 3.5 μU/ml

Fig. 1 Rheumatic disease of the mitral valve. Bleeding in the vasculated leaflets resulting from the resuscitation attempts

The autopsy revealed an adiposity with a body weight of 80 kg and body length of 170 cm, a fatty liver and a struma with a diffusely enlarged left lobe and status after ectomy of the right lobe. Histological examination revealed changes similar to Graves' disease. Signs of exsiccosis and significant coronary artery disease were excluded. The heart demonstrated a rheumatic disease of the mitral valve with fusion of the commissures, fibrosis and vascularisation of the leaflets and shortening and thickening of the chordae tendineae. As a consequence, a moderate hypertrophy of the left ventricle and atrium, a fibrosis of the endocardium and a chronic dilatation of the left atrium were observed (Fig. 1). The heart weight was 420 g and the left ventricle wall was 1.4 cm in thickness. Histologically, blood vessels, scattered lymphocytes, plasma cells and histiocytes were found in the mitral valve.

The examination of the CCS (Hudson 1963; Pomerance and Davies 1975) revealed a continuous interstitial inflammation of the AV-node, the bundle branches and most severely of the His-bundle. The sinus node was inconspicuous. The infiltrates contained abundant granulocytes, histiocytes and lymphocytes (Figs. 2–4). Immunohistochemistry of C5b-9 revealed no necrosis in the CCS but single cell necrosis of the inner layer of the left ventricle. A myoglobin depletion in the CCS was also not detected immunhistochemically (Fig. 4) (Monoclonal antibody Anti-C5b-9, DAKO, primary antibody dilution 1:40; anti-myoglobin antibody, DAKO, primary antibody dilution 1:1000) using the method described by Ortmann and Brinkmann (1997).

Discussion

The clinical symptoms of myocarditis and thyrotoxicosis can be similar, therefore it is easy to attribute the symptoms to both disturbances. But the high blood pressure, the hyperplasia of the partially resected thyroidea, and especially the elevated hormone levels (Table 1) show hyperthyroidism to be a further pathogenetic factor. T4 tends to fall irregularly during the postmortem period and the postmortem levels of T3 are variable, thus T3 seems to be an unreliable marker for detecting hyperthyroidism (Rachut et al. 1980). In our case the blood concentration of T4 and possibly of T3 immediately before death could have been higher than 3 days before and 8 h after death (Coe 1973). However, a long period of hyperthyroidism seems to be unlikely considering the relatively high body weight of the patient.

The comparison of the ECGs recorded 3 days and 16 months before death revealed changes which could be correlated with the inflammation of the CCS (Fig. 5). A tachycardia of 120 beats/min only a few days before death did not result in a shortening of the P-Q time as would have been expected but on the contrary, a prolongation was observed. Functionally, the P-Q time represents the excitement of the left and right atrium, the AV-node together with the His-bundle and branches. The interstitial inflammation had obviously caused the conduction disturbances. Nevertheless in the last ECG recorded 3 days ante mortem, a significant P-Q prolongation could only be detected by comparison with the previous ECG.

Thyroid hormones may influence the oxygen supply and demand by increasing the blood pressure, the heart

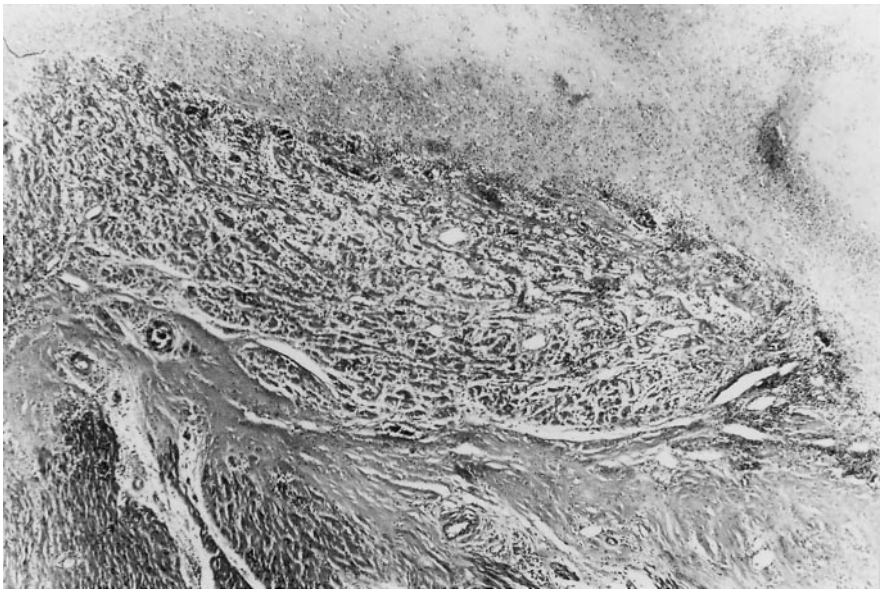

Fig. 2 Penetrating His-bundle shows interstitial edema and mixed infiltrate. Inflammation cells are also seen in the fibrous body close to the bundle (HE, magnification × 25)

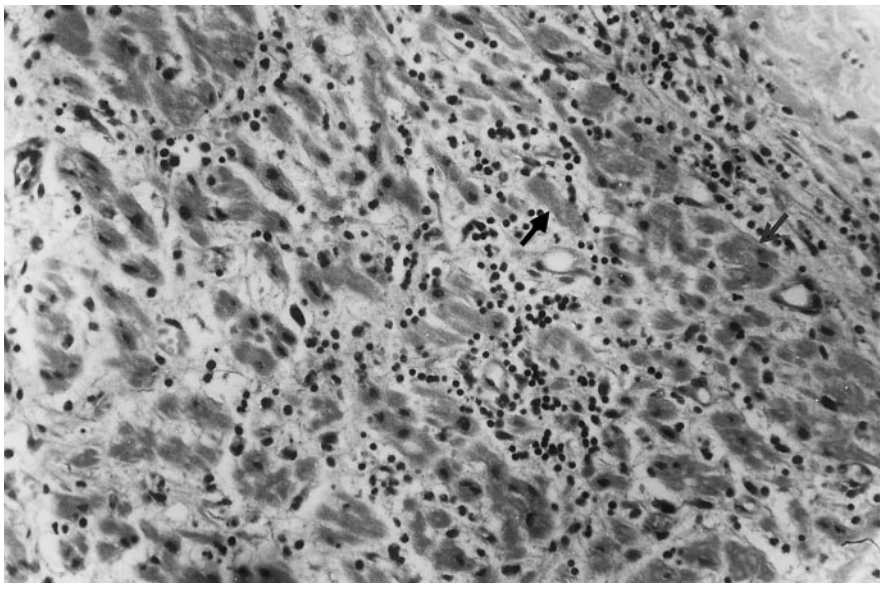

Fig. 3 Absence of necrosis of the His-bundle myocytes. Degenerative changes with vacuolisation (↑). Mixed interstitial inflammation, in other areas granulocytes were more abundant (HE, magnification × 200)

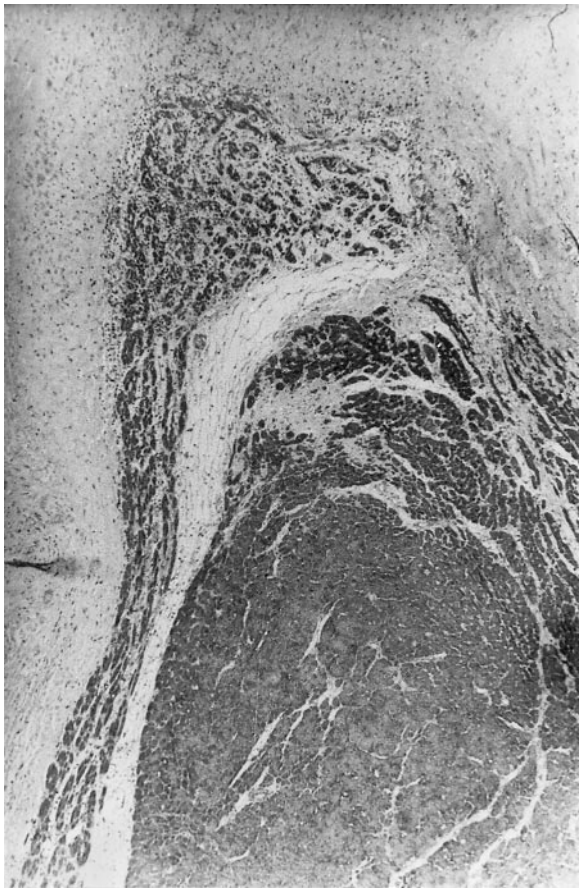

Fig. 4 Inflammation of the branching bundle (*top*) and the left branch (*left*). Infiltrates were absent in the ventricular musculature. No depletion of myoglobin in the CCS could be detected (Anti-myoglobin 1:1000, × 25)

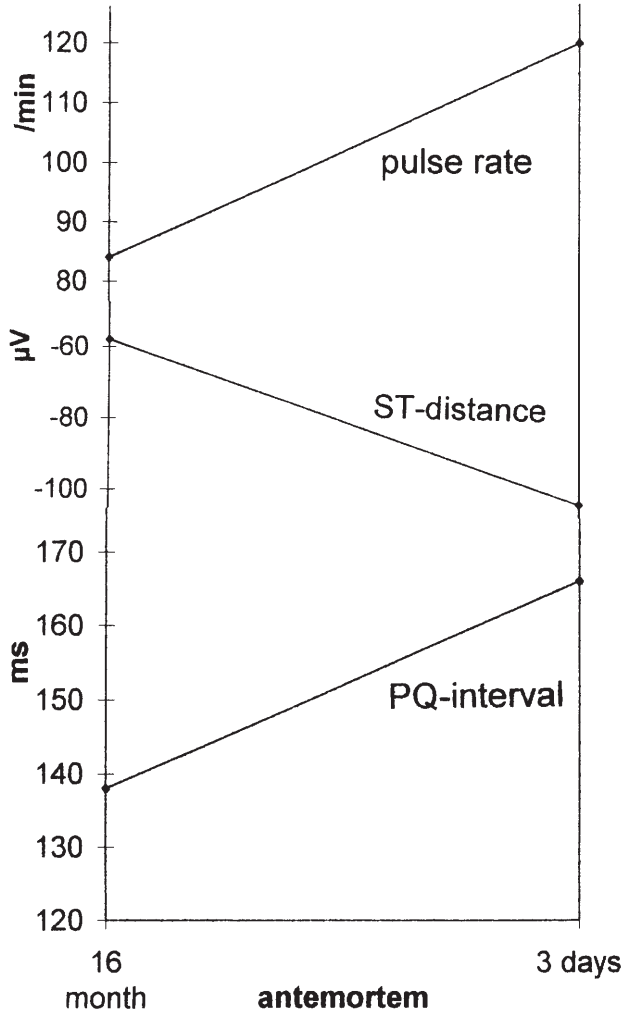

Fig. 5 The comparison of the ECG recorded 3 days and 16 months before death revealed changes of the back-formation of the excitement with horizontally lowered ST-distance in V6 and, in contrast to the tachycardia, a P-Q prolongation

rate and contractile state (Nakano et al. 1987). The positive immunohistochemical findings in the inner layer of the left ventricle could have resulted from such an imbalance between the supply by the coronary circulation and

oxygen consumption leading to myocardial ischemia and single cell necrosis and also indicated by horizontally lowered ST-distances. The presence of ischemic heart disease is not uncommon in thyrotoxicosis.

The etiology of the inflammation of the CCS could not be elucidated in detail (Zack and Wegener 1994) but a viral origin cannot be excluded from the clinical data and histological findings. Most cases of viral myocarditis are not characterised by any specific features but often necrosis of individual muscle fibres together with an infiltrate in the adjacent areas can be detected (Aretz et al. 1987; Billingham 1987; Olsen 1987). In our case, specific myocytes exhibited degenerative changes with vacuolisation (Fig. 3) and the negative immunohistochemical findings underlined the absence of necrosis (Brinkmann et al. 1993). Viral myocarditis mainly affects the working myocardium and an accompanying inflammation of the CCS can sometimes be seen (Pomerance and Davies 1975), but myocarditis confined specifically to the CCS has also been described (Sevy et al. 1968). A rheumatic genesis seems unlikely considering the composition of the infiltrate and lack of fibrinoid necrosis in the CCS. At this time the etiology of an endocrine-induced inflammation of the CCS is speculative, but some investigators found a myocarditis in association with hyperthyroidism (Batsakis 1968; Friedberg 1972; Nora and Flaxman 1943). Careful investigations of the CCS in related cases should reveal whether thyroid hormones alone can cause an interstitial inflammation of the CCS.

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