42 Endocrine and Metabolic Manifestations of Tuberculosis

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42.1 Introduction

Tuberculosis (TB) is often termed ‘a great mimicker’, as it can affect almost any organ in the human body and present in a variety of ways. The endocrine system is no exception, though the incidence of clinical disease is very low. The occurrence of extrapulmonary tuberculosis appears to be increasing in the developed world and is probably a reflection of the impact of HIV infection. Endocrine dysfunction in active tuberculosis results from either a direct affliction of the organs with the disease (endocrine tuberculosis) or more commonly as an abnormality of circulating hormones as a consequence of systemic disease. The latter results from the effects of malnutrition, cytokines and other inflammatory mediators on the hypothalamic–pituitary axis, hormone binding proteins and peripheral metabolism of hormones.

42.2 Endocrine Tuberculosis

Endocrine tuberculosis is uncommon. It may affect any endocrine organ and is the result of organ seeding following hematogenous spread or contiguous spread from a nearby-affected structure. Hematogenous dissemination of virulent tubercle bacilli can occur during the course of primary infection or long after the initial infection. Its clinical manifestation may be part of the systemic disease or may be the sole manifestation of the condition. This chapter deals with tuberculosis affecting the adrenal, thyroid and pituitary glands. Tuberculosis of the gonads is covered elsewhere (chapter 39). Direct tuberculous involvement of the parathyroid glands and the pancreatic islets is extremely rare.

42.2.1 Adrenal Tuberculosis

Primary adrenal insufficiency (PAI) secondary to bilateral adrenal destruction by tuberculosis, was originally described by Addison in 1855. In a review of his eleven patients with adrenal insufficiency seven had tuberculosis. In the past when the disease was rampant and untreatable, tuberculosis was the commonest cause of PAI accounting for 70–80% of the cases (Guttman 1930). With the development of effective chemotherapy and early treatment, tubercu-
losis has increasingly become less common as a cause of PAI and presently contributes from 7–20% of the cases (Nomura et al. 1994; Oelkers 1996). Tuberculous PAI is still thought to be a major cause of PAI in countries like Saudi Arabia where the disease is common. However, in a series of 15 new adult patients diagnosed with PAI since 1982 at the Riyadh Armed Forces Hospital tuberculosis could only be established in three as a cause.

Adrenal involvement occurs from hematogenous seeding. The adrenal glands are especially vulnerable because of their rich blood supply and immunosuppressive effects of high local production of corticosteroids. In an autopsy series of patients with late generalized tuberculosis, adrenal seeding was seen in 53% of patients (Slavin et al. 1980). This is not necessarily associated with clinical disease. Both adrenal glands are involved, though they may not be equally affected. Seeding is followed by an inflammatory reaction which if unchecked causes gradual destruction of the glands. About 90% destruction of both adrenal glands is required before the onset of clinical adrenal insufficiency. Destruction of the adrenal medulla is more common than that of the adrenal cortex (Guttman 1930). The clinical manifestations, however, are related to the deficiency of adrenal cortical hormones. All the layers of the adrenal cortex are affected but as the zona glomerulosa consists of scattered cell groups rather than being a distinct layer, it may be initially only partly destroyed, so that the clinical manifestations may be solely those of glucocorticoid deficiency.

The histology of adrenal TB is no different from any other organ affection (see Chapter 10 on Pathology for details). Earlier in the course of disease there is inflammatory cell infiltration followed by granuloma formation resulting in adrenal gland enlargement. As the disease progresses micro-abscess formation and tissue necrosis occurs. Mass lesions may develop secondary to cold abscesses. With progressive destruction, the glands are gradually replaced by caseous nodules and fibrosis so that after about two years they become normal, or small, in size and ultimately over time they become fibrosed and calcified (Vita et al. 1985).

The clinical features of adrenal TB are similar to those of any other cause of primary adrenal insufficiency. These include weakness, fatigue, weight loss, abdominal pain, diarrhea, hyperpigmentation and orthostatic hypotension. There may be associated fever and abnormal mental activity. The laboratory tests show hyponatremia, hyperkalemia, azotemia, anemia and eosinophilia. The clinical syndrome may accompany active systemic disease such as acute pulmonary, miliary or other extra-pulmonary tuberculosis (Alvarez and McCabe 1984). More commonly as adrenal destruction is a slow process the clinical presentation occurs as an isolated entity years after the initial infection (Nomura et al. 1994; Sanford and Favour 1956; Vita et al. 1985). Rarely the presentation is that of an adrenal mass (unilateral or bilateral) seen on CT of the abdomen (Jayakar et al. 1998). Whereas the presentation is insidious, patients may occasionally present with an acute adrenal crisis following the use of rifampicin (Elansary and Earis 1983).

The diagnosis of adrenal insufficiency is confirmed by demonstrating a decreased, or absent, cortisol response to exogenous ACTH (synacthen stimulation test). Elevated ACTH levels and associated mineralocorticoid deficiency confirm that the adrenal insufficiency is due to adrenal destruction. Mineralocorticoid deficiency is characterized by hyponatremia and hyperkalemia and confirmed by findings of high renin and low aldosterone levels. Once a hormonal diagnosis of PAI is made the next step is to determine its cause. A supportive CT scan, or MRI of the adrenal glands, absence of adrenal antibodies and other causes of this disease are required to support TB as the cause of PAI (Lauret et al. 1998). The presence of extra-adrenal TB is highly supportive. A final diagnosis requires either histological proof or positive tissue cultures. Although not performed routinely a CT-guided needle biopsy of the adrenals can provide diagnostic material and is useful in doubtful cases. It is of great value during investigation of unilateral or bilateral adrenal masses (Yee et al. 1986).

42.2.1.1 CT Features of Adrenals Tuberculosis

CT plays a major role in diagnosis of established tuberculous adrenal disease (Hauser and Gurret 1986; Villabona et al. 1993; Wang et al. 1998; Wilms et al. 1983). The appearance of the adrenals on CT will vary depending on the stage of disease. Adrenal enlargement has been commonly documented during routine screening in pulmonary tuberculosis. It is more likely to occur with acute pulmonary TB, rather than chronic pulmonary disease (Kelestimir et al. 1994). An enlargement of the adrenals seen in patients with pulmonary tuberculosis during routine CT probably represents stress related hyperplasia or adrenalitis and not clinical disease (Gulmez et al. 1996; Kelestimir et al. 1994). The following presentations are well recognized in tuberculous adrenalitis.