Abstract

Malakoplakia is an unusual chronic inflammatory disease occurring predominantly in the bladder and kidney [2] and only rarely affecting other organs. For the urinary tract, its aetiology has been ascribed to the presence of Escherichia coli, while the very few cases of cerebral malakoplakia which have been reported so far, have mostly occurred in infants in the clinical setting of neonatal herpes virus infection or otherwise in adults in areas of cerebral infarction. We here report a case of E. coli-associated malakoplakia of the brain. It occurred in a 53-year-old man who had undergone long-term corticosteroid therapy and had previously been operated on a cerebral E. coli-associated abscess. This case indicates that malakoplakia of the brain might also be a histiocytic reaction against bacterial antigens of the E. coli family.

Key words: Cerebral malakoplakia · Central nervous system · Michaelis-Gutmann bodies · Herpes simplex encephalitis · Escherichia coli

Introduction

Malakoplakia is an unusual chronic inflammatory disease occurring predominantly in the bladder and kidney [2] and only rarely affecting other organs like the testes [24], the endometrium [25], the gastrointestinal tract [17], the lung [23], the skin [15] or the peridontium [22]. Most cases of malakoplakia have been limited to one organ; however, multifocal involvement of kidney, bladder and skin has also recently been reported [15]. So far, very few cases of cerebral malakoplakia have been documented, most of them in infants and mainly in the clinical setting of neonatal herpes virus infection [7, 8, 11, 21, 28] or occurring in areas of cerebral infarction [4, 10]. Regardless of its location, malakoplakia may clinically simulate a neoplastic growth [26]; accordingly, Michaelis and Gutmann, in their first description of this entity, proposed that it may represent a benign tumour of the bladder [20]. Malakoplakia can only be determined histopathologically and the decisive morphological finding in its diagnosis is the presence of typical concentric cytoplasmic histiocytic inclusions, the mature Michaelis-Gutmann (MG) bodies.

We present the case of a 53-year-old man suffering from cerebral malakoplakia secondary to the earlier removal of an Escherichia coli-associated cerebral abscess.

Clinical history

In November 1997, a 52-year old diabetic man was diagnosed as suffering from dilated cardiomyopathy with mild insufficiency of the mitral valve. An atrial thrombus was discovered and the patient subsequently received anticoagulant warfarin therapy. Half a year later, in May 1998 and at the age of 53 years, the patient suffered a right-sided temporo-parietal intracerebral haemorrhage with contact to the ventricular system. Due to the poor condition of the patient, this was treated conservatively with insertion of a ventricular shunt and high-dose corticosteroid therapy to reduce cerebral oedema. In early July 1998, 7 weeks after the cerebral haemorrhage, the patient developed bacterial meningitis, on several occasions showing E. coli in both cerebrospinal fluid and bronchial lavage. During hospitalisation a cerebral computed tomography scan revealed encephalitic changes with several intracerebral lesions. Initial biopsy of one of these lesions in July 1998 revealed a subacute to chronic intracerebral haematoma undergoing organisation. A second biopsy 3 weeks later, in August 1998, was gained from a right-sided occipital lesion which preoperatively had been diagnosed as an abscess; it was subsequently partially removed and sent for neuropathological diagnosis (Fig. 1). Postoperatively, the patient recove-
Malakoplakia is an uncommon chronic inflammatory lesion which is morphologically characterised by the presence of laminated calcospherules, so-called MG bodies; their presence in mononuclear phagocytes (termed von Hansemann’s histiocytes) has been considered pathognomonic for malakoplakia. MG bodies, however, have also been found in an extracellular location as seen by Ho [12], McClure [18] and us.

Ultrastructurally, macrophages exhibit membrane-bound phagolysosomes containing whorled and parallel lamellar phospholipids; the initial stage of calcification appears to be the deposit of apatite crystals within intracytoplasmatic membrane-bound vesicles of histiocytes followed by an accumulation of these apatite crystals and coalescence of calcified vesicles resulted in the formation of MG bodies [2]. According to August et al. [2], the concentric arrangement of phagolysosomes is important for mineralisation and formation of MG bodies; their targetoid structure resulted from the initial mineralisation of matrix cores and the separate mineralisation of peripherally arranged, continuously accumulated phospholipids and microvesicles which probably represent nondigestive debris. These stages of “maturation” also account for the varying staining intensity of MG bodies within one case. Malakoplakia usually affects the urinary bladder but is increasingly found elsewhere [4]. The development of malakoplakia has been ascribed to two main aetiological features: several studies have suggested that coliform organisms play a role in the pathogenesis of this disorder [9, 19]; all five cases described by August et al. [2] had a history of E. coli infections, two of which were associated with bacteraemia. Moreover, immunological abnormalities may be an accompanying secondary factor responsible for altered reactivity of macrophages and lysosomal disturbance [2]. Lou and Teplitz [16] suggested a defect in the macrophagic lysosome which could lead to incomplete cell degradation resulting in the deposition of products incompletely digested, thus causing malakoplakia; recently, functional and morphological abnormalities have also been found in monocytes [27]. Associations of malakoplakia with immunocompromising systemic diseases like AIDS [23], autoimmune thyroiditis [6], lupus erythematosus [29], tuberculosis and sarcoidosis [5] as well as with malignant neoplasia [13], diabetes mellitus and alcoholism [14] have also been reported. Furthermore, disturbances in T lymphocytes or cell-mediated immunity have been implicated in the pathogenesis of malakoplakia as it tends to occur in patients treated with immunosuppressive drugs [3]. Our patient fitted at least two of the above features by suffering from diabetes mellitus and undergoing corticosteroid therapy at the same time.

Malakoplakia of the brain is extremely rare and only nine cases have been reported so far: six of these involved neonates and infants between the ages of 3 weeks and just under 3 years and were associated with neonatal herpes simplex infection [7, 8, 11, 21, 28]. However, in most cases

Neuropathological findings

The sample of the second operation consisted of several dark-brown tissue specimens of a combined size of 5.3 × 3.1 × 1.0 cm and a weight of 8 g. The cut surface was of a spotty yellow hue. The tissue was formalin-fixed, paraffin-embedded and cut into sections of 8 μm. The cut surface was subsequently stained with haematoxylin-eosin, elastica-van Gieson, periodic acid-Schiff’s reagent (PAS), Congo and Prussian blue as well as according to Gram and Grocott.

Histologically, the specimen was characterised by chronically inflamed brain tissue with dense infiltrates consisting of lymphocytes, plasma cells, neutrophilic granulocytes, macrophages and collections of mononuclear phagocytes. Mesenchymal organisation by fibroblasts, neovascularisation and collagen fibres as well as occasional haemosiderin and haematoidin deposits could be seen. Furthermore, there were necroses of both the inflamed tissue and the brain tissue. Areas containing many macrophages showed numerous Michaelis-Gutmann (MG) bodies of 7–10 μm in diameter and targetoid shape. These bodies were positive for PAS and Prussian blue and weakly argentophilic after staining with Grocott dye (Fig. 2). Most of the MG bodies were extracellularly distributed within the tissue; some, however, were found – often in high numbers – in the cytoplasm of macrophages. No bacteria or fungi were demonstrated. The diagnosis was that of a subacute to chronic, partly abscess-forming encephalitis with numerous MG bodies, indicative of cerebral malakoplakia.

Discussion