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CASE REPORT

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Neglect-associated fatal Marchiafava-Bignami disease in a non-alcoholic woman

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Abstract We present the case of an 80-year-old malnourished and non-alcoholic woman who died from neglect-associated Marchiafava-Bignami disease, an illness usually almost exclusively occurring in male alcoholics. The patient had been bedridden for several months and had been looked after by her son. The patient was admitted to hospital in an extremely poor care condition suffering from severe exsiccosis, pressure sores and marasmus and died shortly afterwards. The initial post-mortem examination could not establish a definite cause of death, however, upon neuropathological examination a necrotising cystic lesion in the left cingulate gyrus as well as a central necrosis in the corpus callosum indicative of Marchiafava-Bignami disease were revealed. This is the first known case of Marchiafava-Bignami disease in a non-alcoholic woman and the first case in the forensic setting of neglect.

Keywords Marchiafava-Bignami disease · Non-alcoholic · Female · Malnutrition · Neglect

Introduction

Marchiafava-Bignami disease is an extremely rare condition characterised by a demyelination of the corpus callosum which almost exclusively occurs in male alcoholics (Harper and Butterworth 1997; Kohler et al. 2000). Its prevalence in France has been estimated to be 0.21% (Hauw et al. 1988) while in Australia, Marchiafava-Bignami disease has only been diagnosed once in approximately 10,000 brains associated with alcohol-related disorders (Harper and Kril 1993). Marchiafava-Bignami disease was originally described in Italian red wine drinkers (Harper and Butterworth 1997) but has subsequently been described in drinkers with abuse of other alcoholic beverages (Ishizaki et al. 1970; Ghatak et al. 1978), with very few female alcoholics among them (Walter 1978). Marchiafava-Bignami disease in non-alcoholic patients is even rarer and has so far only been encountered in males (Koeppen and Barron 1978; Leong 1979; Ma and Chen 1983; Kosaka et al. 1984) and only one of these in the setting of malnutrition (Leong 1979). However, non-alcoholic women suffering from Marchiafava-Bignami disease have hitherto not been described.

We report the first known case of Marchiafava-Bignami disease in a non-alcoholic woman, in whom the illness was presumably caused by malnutrition associated with neglect.

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Case report

Clinical history

An 80-year-old female with a history of diabetes mellitus, nephrotic syndrome, cardiac failure (NYHA II) and arterial hypertension, had been bedridden for several months. The patient had previously been admitted to hospital in September 1999 and January 2000 for a stroke in the right basal ganglia which manifested itself clinically in weakness, aphasia, deviation of the tongue to the left and drooping of the left corner of the mouth. CT investigations had shown an infarction in the right caudate nucleus and putamen. The corpus callosum had appeared normal. Subsequently, she had been looked after by her son who lived in the same apartment. The patient was readmitted to hospital in August 2000 in extremely poor care condition with soiling all over the body and additional excrement on the trunk. She suffered from severe exsiccosis and marasmus and showed contractures of the knee and hip joints which could not be moved. Multiple superinfected pressure sores were found in the sacral region, around the hips, the right shin and both feet. An amputation of the left thigh and debridement of necrotic tissue from the left foot were planned; however, the patient died in hospital before these procedures could be undertaken.

The son who was present at hospital admission had 6 months previously refused to send his mother into an institutional care facility or to use a home help because he wanted to look after his mother himself. The mother had not seen a physician since having been discharged from hospital in February 2000 and the son was

not able to divulge any information on his mother's neurological or psychiatric status.

Autopsy results

The initial forensic autopsy revealed the following:

- Signs of neglect over a long period: soiling all over the body and superinfected pressure sores, gangrenous left foot, contractures of knee and hip joints, dirty finger and toe nails with fungal infections.
- Severe marasmus (body weight 46 kg, body height 170 cm): atrophy of the subcutaneous fatty tissue, the skeletal muscles and the parenchymatous organs.
- Exsiccosis with dry fatty tissue, skin folds remaining elevated, dry and scabby tongue.
- Addional findings: generalised arteriosclerosis, left ventricular hypertrophy, pulmonary emphysema, arterio-/arteriolosclerosis of both kidneys.

Cause of death. No definite cause of death could be established after autopsy.

Neuropathology findings

The subsequent neuropathological examination revealed:

- Macroscopically: necrotising cystic lesion in the left cingulate gyrus (2.5 × 1.2 × 0.3 cm) and yellow-brownish discolouration

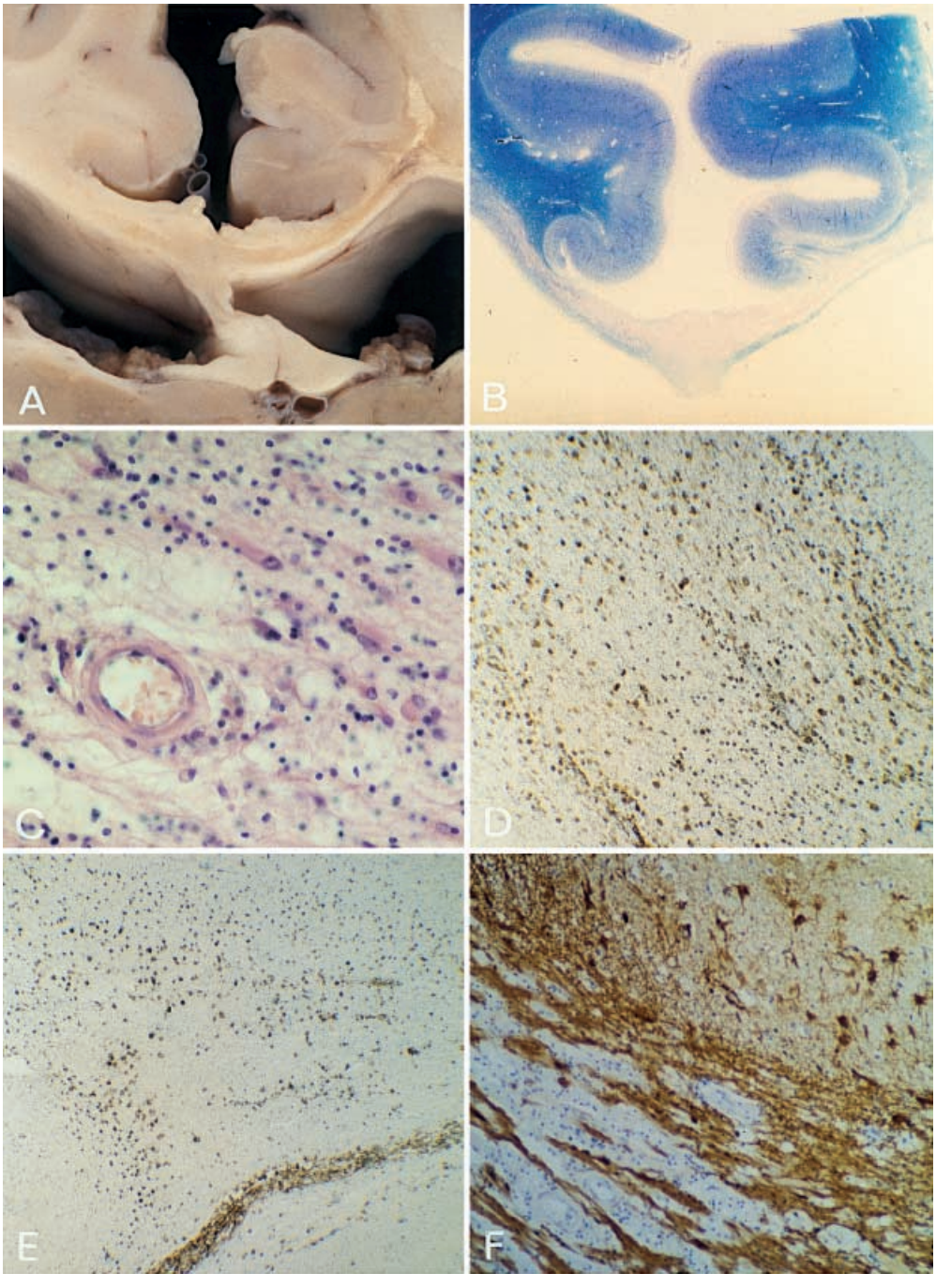

Fig. 1 **A** Macroscopical aspect of Marchiafava-Bignami disease with necrotising cystic lesion in the left cingulate gyrus and yellow-brownish discoloration with central necrosis along the length of the thinned corpus callosum. **B** Demyelination *(pale)* of corpus callosum mainly affecting the central fibres with preservation of the thin upper and lower edges ("sandwich" lesion) as well as the left cingulate gyrus compared with normal white matter (*dark blue*; Klüver-Barrera stain for myelin, original magnification 1.4 ×). **C** Demyelination, macrophages and gliosis with relative sparing of the axons in the central corpus callosum. Blood vessels show proliferation and hyalinisation of the walls (HE, original magnification 80 ×). **D** Abundant macrophages in the centre of the corpus callosum while upper and lower edges are hardly affected (*bottom left and top right*; KiM1P, original magnification 8 ×). **E** Abundant macrophages and reactive microglia cells in the corpus callosum *(bottom right)* and cingulate gyrus (*top left*; KiM1P, original magnification 8 ×). **F** Astrocytes show only mild reactive changes but are prominent around necrotising lesions *(top right)*; lipid-laden macrophages in the centre of the corpus callosum remain unstained (*bottom left*; GFAP, original magnification 80 ×)

with central necrosis along the length of the thinned corpus callosum (Fig. 1 A). Staining with Klüver-Barrera for myelin revealed severe demyelination in the left cingulate gyrus and the corpus callosum, in the latter mainly affecting the central fibres with preservation of the thin upper and wider lower edges ("sandwich" lesion; Fig. 1 B).

– Microscopically: predominant demyelination with relative sparing of the axons in the corpus callosum, reduced oligodendrocytes and abundant lipid-laden macrophages (Fig. 1 C). Immunohistochemistry for the macrophage/microglia marker KiM1P and glial fibrillary acidic protein (GFAP) revealed abundant macrophages and activated microglia in the corpus callosum (Fig. 1 D, E) and cingulate gyrus (Fig. 1 E), upper and lower edges of the corpus callosum were hardly affected (Fig. 1 D). Astrocytes showed only mild reactive changes but were prominent around necrotising lesions (Fig. 1 F). Blood vessels presented proliferation and hyalinisation of the walls (Fig. 1 C).
– Additional findings: normal brain weight (1309 g), arteriosclerosis of basilar and both medial cerebral arteries, cystic lesion (infarction) in the right neostriatum (putamen and caudate nucleus $2.8 \times 1.7 \times 0.6$ cm).

Cause of death. Necrosis of the corpus callosum (Marchiafava-Bignami disease).

Discussion

Marchiafava-Bignami disease is characterised by necrotising, often cystic lesions of the corpus callosum. Involvement is generally maximal in the genu and body, but can also be seen in the anterior commissure, centrum semiovale and middle cerebellar peduncles or, as in this case, in the cingulate gyrus. Microscopically, there is predominant demyelination with relative sparing of the axons. In the corpus callosum, mainly the central fibres are affected with preservation of the thin upper and lower edges giving the lesion a "sandwich" appearance. The pathogenesis of Marchiafava-Bignami disease is still unknown but there are similarities in the pathology with cyanide intoxication and some cases of carbon monoxide poisoning (Harper and Butterworth 1997). Furthermore, its association with alcohol abuse and occurrence in the setting of malnutrition show that the underlying cause is metabolic.

There is no stereotypical clinical presentation of Marchiafava-Bignami disease, however, the symptoms are more severe than the pathological lesions would predict. Altered mentation, depression, mania, paranoia or dementia, is soon accompanied by seizures, hemiparesis, aphasia, ataxia, dysarthria or abnormal movements, often progression to death within weeks or months (Kohler et al. 2000). Two major clinical pictures are evident: an acute form with seizures and disorders of consciousness progressing to death, or a more chronic form with progressive dementia or interhemispheric disconnection syndromes which may last several years. The diagnosis, as in this case, is often not made until autopsy, but cases have been diagnosed during life with CT and MRI (Baron et al. 1989; Chang et al. 1992). Lesions can exist subclinically and MRI has revealed callous lesions which, along with the symptoms, even regressed with abstinence (Baron et al. 1989). In the presented case, demyelination must have developed in the 6 months after the second period of hospitalisation because the CCT in January/February 2000 did not show any changes in the corpus callosum. Unfortunately, the mother had not seen a physician since being discharged in February 2000 and the son was not able to divulge any information on his mother's neurological or psychiatric status, so that we can not elucidate the clinical progress and symptoms of Marchiafava-Bignami disease in this patient.

Death in our case most probably occurred as a result of sudden cardiorespiratory failure through necrosis of parts of the limbic system. The nerve supply to the heart and thus control of cardiac function originates in the limbic cortex, in particular in the cingulate gyrus which was severely affected by the lesions typical of Marchiafava-Bignami disease and descends to the hypothalamus, possibly via the basal ganglia, but most likely via the amygdala. From the hypothalamus, the two limbs of the autonomic nervous system then descend with intermediate synapses in cardiopulmonary control centres in the reticular formation of the brain stem where a number of reflexes are mediated. Changes within this chain may lead to reflex disturbance and thus life-threatening and lethal arrhythmias (Rossi 1999). A further potential pathomechanism is subendocardial myofibrillary degeneration involving the cardiac conduction system and thus predisposing to arrhythmias and sudden death which has been generated experimentally by stimulation of the limbic cortex (Samuels 1993).

Neglect and maltreatment of the elderly is a common problem that is estimated to affect more than 3% of this age group (Pillemer and Finkelhor 1988; Tsokos et al. 2000; Ortmann et al. 2001). It occurs within the context of long-term care, and most cases are hidden to others (Meier-Baumgartner and Püschel 1996). The victims usually show typical risk factors such as living together with the abuser, isolation, and dependence on care with the perpetrator depending financially on the victim (Kleinschmidt 1997; Ortmann et al. 2001). All of the above factors were present in our patient.

In conclusion, we present the first case of Marchiafava-Bignami disease in a non-alcoholic woman, in which the illness was presumably caused by malnutrition associated with neglect. Death occurred most likely through cardiorespiratory arrest caused by disturbances of cardiopulmonary control centres secondary to decompensation of cerebral neuronal pathways involving the limbic system.

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