Adult neuronal ceroid lipofuscinosis (Kufs' disease)

A sporadic case

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Summary

A sporadic case of neuronal ceroid lipofuscinosis (Kufs' disease) in a 29-year-old man is reported. At onset the disease resembled schizophrenia (thought disorder, flat affect, paranoia, hallucinations and inappropriate behaviour), but after the appearance of associated neurological symptoms such as myoclonic jerks, cerebellar ataxia, rigidity and involuntary movements a neurological disorder was suspected. Cortical biopsy established the diagnosis.


At the turn of the century, the syndrome of amaurotic familial idiocy included inherited progressive neurological disorders with some clinical features in common (intellectual deterioration, seizures, loss of sight and fatal outcome). They were classified according to age of onset and given a variety of eponymous labels (Batten's disease, etc.). The term neuronal ceroid lipofuscinosis was introduced by Zeman and Dyken in 1969 to include all forms of amaurotic familial idiocy except Tay-Sachs disease (after it was found that the stored material in Tay-Sachs disease was ganglioside and this form became recognized as a separate entity). In all other forms of amaurotic familial idiocy there is no altered ganglioside metabolism but rather intraneuronal accumulation of ceroid and lipofuscin.

The diagnosis of neuronal ceroid lipofuscinosis is based on demonstration of excessive intraneuronal, astrocytic and visceral accumulation of autofluorescent granules which have been defined ultrastructurally and histochemically as ceroid and/or lipofuscin. The biochemical pathogenesis of this disorder is still unknown.

Neuronal ceroid lipofuscinosis can be divided into various subtypes according to phenotypical criteria. Boehme et al. described several such types, including the Kufs type which has erroneously been named 'adult familial amaurotic idiocy'.

Case report

A 29-year-old accountant, married with 1 child, the eldest of 3 children of a Jewish family, was referred to the psychiatric outpatient unit at the Johannesburg Hospital because of progressive mental deterioration, frequent psychotic episodes and difficulties in concentration and in daily functioning for the previous 3 months.

His birth had been normal, but at the age of 3 months he was operated on for pyloric stenosis. After this his health had been good and his development normal. He had worn spectacles from early childhood. He had been a very sociable and friendly child and later maintained good relations with his family, especially his father and younger brother. He described his mother as a very warm person giving him at times too much love. Towards his sister he was cool.

At the age of 20 the patient studied accountancy. After he had graduated he worked for an industrial firm, but was asked to leave 2 months later. He never understood the reason for this decision. While travelling in Europe at the age of about 27 he met his future wife, whom he liked 'because of her nice eyes, her political opinions and her interesting philosophy of life'. They were married in Johannesburg 2 months later and shortly afterwards developed a common theory of living on a different planet and became very close to each other.

They had a baby, but the wife refused responsibility for it and her behaviour became bizarre. She asked the patient to have her admitted to hospital but he refused, arguing that all her problems were due to developmental problems in childhood. He promised that she would be cured through his love. He decided to stay at home, care for the child, and take all the home responsibilities on himself.

His wife attempted suicide and he brought her to the hospital casualty unit, where she was seen by a psychiatrist who decided that her husband also needed psychiatric assessment. His family history was negative for neuropsychiatric illnesses. A month later he was admitted to hospital.

His complaints had begun 3 months before admission, when he started having difficulty in concentrating. His memory deteriorated rapidly and he stopped working and stayed at home all day, attributing his problems to the fact that he had stopped wearing his spectacles.

Because of the difficulties of keeping a married couple in the same ward and the possibility of a folie à deux it was decided to treat him as an outpatient. Thoridiazine 25 mg 3 times a day was prescribed. During his last outpatient visit he showed a flat affect combined with inappropriate laughing, was partially disoriented and disclosed paranoid thoughts. After his wife improved and was discharged 3 weeks later, it was decided to admit him for further investigations.

On admission the patient was confused and very tense, with thought blocks and memory lapses, and his affect was inappropriate. His blood pressure was 120/80 mmHg and his pulse rate 78/min. No medical or neurological abnormality was detected. Results of a full blood count and the serum protein, electrolyte, glucose, urea and creatinine levels were all within the normal range, and liver function was normal. The erythrocyte sedimentation rate was 18/43 mm/1st h, the Wassermann reaction was negative, and analysis showed the CSF to be normal. Neurological examination repeated a week later revealed a mild hyperreflexia on the right side and a possible positive Babinski sign on the right. The EEG indicated a diffuse encephalopathy. A repeat wake and sleep EEG showed diffuse...
bursts of spikes and spike-wave complexes, and bilateral synchronous paroxysms of triphasic bursts, compatible with a diffuse encephalopathy (grey matter disease) (Fig. 1). He was given chlorpromazine 100 mg 3 times a day, but his mental state deteriorated progressively. He developed urinary and faecal incontinence, and lost orientation for time and space. Short episodes of myoclonic jerks and gait disturbance were noted. He began talking of auditory hallucinations and blaming his wife for his condition. On the following day bizarre involuntary movements were noted and he became rigid. Brain biopsy was performed and tissue from the right frontal lobe showed a mild neuronal loss in the cerebral cortex with normal white matter and no inclusion bodies. Pigment granules were present in neurons in sections stained with periodic acid-Schiff. The stored material was granular, brown-yellow in colour and autofluorescent in unstained sections. Under the electron microscope the stored material was revealed to be membrane-bound, granular, dense, osmiophilic, and occasionally formed by irregular, packed rectilinear profiles; this was compatible with a diagnosis of neuronal ceroid lipofuscinosis (Kufs' disease) (Fig. 2).

**Discussion**

Kufs' disease, an adult form of neuronal ceroid lipofuscinosis, is very rare and fatal, common with autosomal recessive inheritance. Kufs' disease covers a broad spectrum of clinical manifestations. Two types, in which a cerebellar syndrome or extrapyramidal signs predominate, were mentioned by Seitelberger and Nagy. The most common symptoms are dementia, cerebellar ataxia, involuntary movements, rigidity, myoclonus and seizures. Visual symptoms are usually not present. The condition becomes manifest at the age of about 30 years and is ultimately fatal, average survival from the time of onset being 7 years. The most prominent abnormal histological findings involve the cerebral cortex, cerebellum, substantia nigra, and various other subcortical nuclei.

The combination of progressive dementia, myoclonic jerks, progressive cerebellar ataxia and involuntary movements should suggest the possibility of a cerebral lipidosis. It is important to distinguish this from two other disorders in which symptoms are similar: (a) Lofra body disease, characterized by onset in the 2nd decade, rapidly progressive intellectual deterioration, myoclonus epilepsy and parental consanguinity; and (b) the so-called dysynergia cerebellaris mylonica, involving the olivodentate system and usually with onset from the 2nd decade onwards.

Neurolipidoses causing progressive dementia in adults are rare in comparison with those in children. Several cases of late manifestation of cerebral lipid storage disease have been reported recently. Through the development of electroencephalographic analysis, supplemented by electroretinography and cortical visually evoked potential studies in recent years, early diagnosis of these conditions, even in the presymptomatic phase, is possible. Neurolipidoses, although rare, should always be considered in the differential diagnosis of adults presenting with progressive mental deterioration and cerebellar or extrapyramidal symptoms. They may at times mimic a psychiatric illness (schizophrenia) and should also be considered in the differential diagnosis of acute paranoid states. A routine EEG is therefore recommended in every patient who presents with a history of psychotic episodes, in order to exclude these conditions. Early diagnosis of cerebral lipidosis is of the utmost importance in relation to genetic counselling and the prevention of further family tragedies.

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**REFERENCES**


**Fig. 1. The EEG is abnormal due to bilateral synchronous paroxysms of 100-150 µV of triphasic 3 Hz bursts which occur periodically every 3-5 seconds. The background rhythm shows low amplitude (25 mV), 6-9 Hz. This pattern is frequently seen in cerebral lipidosis.**

**Fig. 2. Electron micrograph showing inclusions of varying size in the cytoplasm of a nerve cell body (dark material). The inclusion bodies are irregular in shape and surrounded by a membrane. They are lysosomes which contain lipofuscin storage material (X 3000).**