

Clinical Article

Right Hemispheric Frontal Lesions as a Cause for Anorexia Nervosa Report of Three Cases

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Summary

Object: Aetiology and pathogenesis of eating disorders is a matter of controversy. In some cases they can occur in association with tumours involving the temporal cortex, in temporal lobe epilepsy or in the advanced state of degenerative diseases involving temporal structures. We report about three patients with right frontal intracerebral lesions, one oligo-astrocytoma and two vascular malformations, associated with partial seizures and anorexia nervosa.

Patients and Methods: 3 patients, one female and two men with anorexia nervosa and right frontal intracerebral lesions were admitted to our wards due to focal seizures or loss of consciousness. They were treated either microsurgically or by endovascular embolization after neuro-imaging. In our retrospective analysis of the patients' reports and course we investigated the histopathology of the lesions, duration of the eating disorder and the clinical outcome.

Results: Two patients underwent craniotomy with extirpation of the lesion. In one case histology revealed an oligo-astrocytoma, in the other haemorrhagic infarction due to a venous malformation. The patient with the arteriovenous malformation (AVM) was embolized with microparticles. The patients with the oligoastrocytoma and AVM totally recovered. They gained weight and stayed seizure free. The patient with the infarction remained in a vegetative state.

Conclusions: Right frontal intracerebral lesions with their close relationship to the limbic system could be causative for eating disorders. We therefore recommend performing a cranial MRI in all patients with suspected eating disorders, especially if they occur in combination with focal seizures.

Keywords: Eating disorder; cerebral; right frontal lobe; seizure; anorexia nervosa; malnutrition.

Introduction

The term anorexia nervosa is coined from the Greek words anorexia – no appetite and nervosa – caused by psychogenic reasons. It describes an entity of malnutrition due to a self limited restriction of food often

combined with vomiting. Most of the patients are young females. The aetiology as well as the pathogenesis is uncertain and a matter of controversy. In general eating disorders can occur in association with tumours involving the temporal cortex, in temporal lobe epilepsy or in the advanced state of degenerative diseases involving temporal structures.

Therapeutic approaches are multifold ranging from psychotherapy, neuroleptic drugs to parenteral feeding.

We report about three patients with right frontal intracerebral lesions, one oligo-astrocytoma and two vascular malformations, associated with partial seizures and anorexia nervosa.

Case Reports

Case 1

A 24-year-old male was hospitalized due to two Grand mal seizures. In the patient's history we found a weight loss of 20 kg during the last 3 years (recent 42 kg/159 cm, Body Mass Index = 16 [BMI; dividing body weight in kilograms by height in meters squared]) due to refusal of food, depression and compulsive studying up to 18 hours a day. Diagnosis was made at a pediatric department for psychosomatic diseases. Patient's former treatment included hypercaloric treatment and group psychotherapy.

Gastroenterological and neurological investigations including EEG, abdominal sonography, endoscopy of the gastrointestinal tract, and recent laboratory parameters did not show any pathology. At least a cranial MRI showed a right frontal intracerebral lesion with contrast enhancement, signs of bleeding and slight perifocal oedema (Fig. 1). The tumour, an oligo-astrocytoma WHO II, was excised with the help of a frameless neuronavigation system (Surgiscope®, Jojumarie, Berlin). Postoperative course was un-

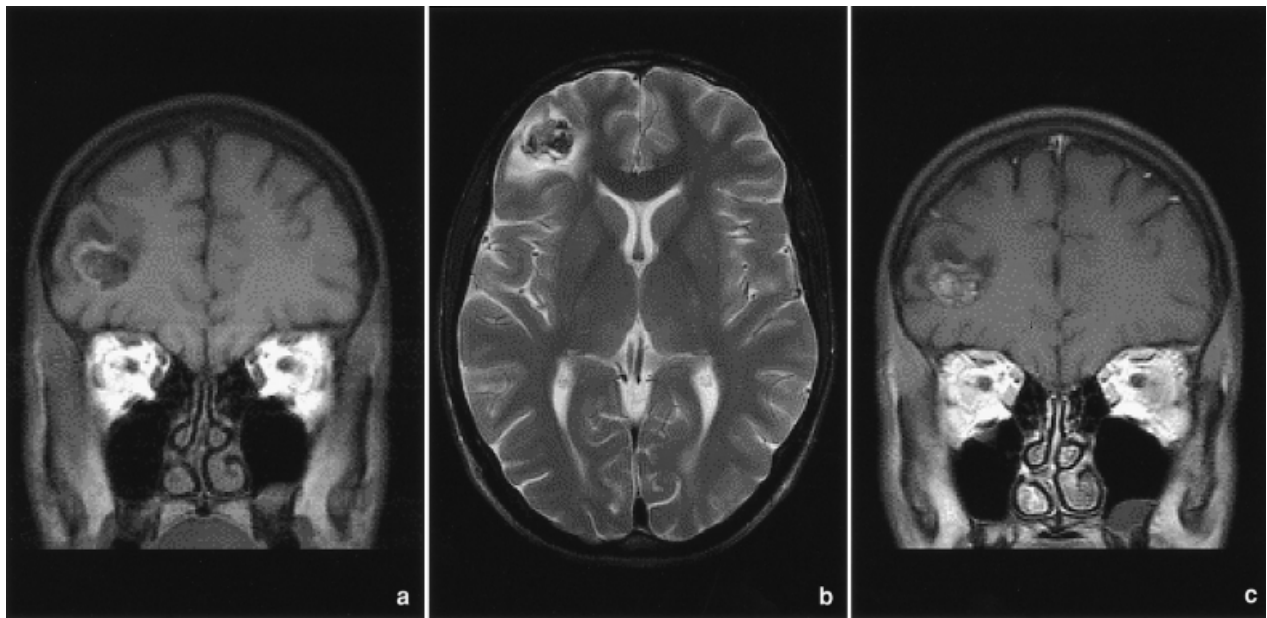


Fig. 1. Frontal oligo-astrocytoma in a 24-year-old man. (a) Unenhanced coronal T1-weighted MRI shows a subcortical, heterogeneous mass (2 cm in maximum diameter) with foci of haemorrhage and surrounding oedema in the right frontal lobe. (b) Axial T2-weighted MRI demonstrates the heterogeneous mass and the surrounding oedema. (c) Contrast enhanced T1-weighted MRI at the level of (a) shows focal enhancement in the inferior aspect of the mass

eventful and the patient was discharged on the 5th postoperative day from our wards. In the routine three months follow up the patient was seizure free without anti-epileptic medication, gained 9 kg of weight and worked again as a teacher. His neurological outcome was grade 5 according to the Glasgow Outcome Scale (GOS) [16] and grade 1 according to Engel [11].

Case 2

A 36-year-old male was hospitalized due to a Grand mal seizure. The suspected reason was a lowered potassium serum level after multiple bouts of vomiting due to his refusal of food, which was diagnosed as anorexia nervosa one year before at a department for psychosomatic diseases. His former treatment included psychotherapy and hypercaloric diet. His recent weight was 48 kg and the height 167 cm (BMI 17). The neurological examination including EEG did not show any pathology. The cranial MRI revealed an AVM with 2.5 cm in diameter located in the right middle frontal gyrus (Fig. 2). The malformation was treated by endovascular embolization. At the three months neurological follow up examination the patient was seizure free without anti-epileptic medication, gained 8 kg of weight and worked again in his job for an insurance company. His neurological outcome was grade 5 according to GOS and grade 1 according to Engel.

Case 3

A 23-year-old girl was admitted to our emergency room due to a sudden drop and consecutive loss of consciousness following a two days episode of headache. After oral intubation an emergency CT showed a right frontal haemorrhagic infarction with severe shift of the midline structures (Fig. 3). The patient was immediately transferred to our operation room and a decompressive craniotomy and resection of the infarcted area was performed. Histology revealed a

venous malformation. In the patient's history we found a four year history of avoidance and refusal of food in combination with compulsive studying and intermittent attacks of fear, which was diagnosed as anorexia nervosa by a psychosomatic pediatric department. Former treatment included hypercaloric diet and psychotherapy in a group and with her family. Her recent weight was 39 kg, the height 155 cm (BMI 16). Menstrual function was described as oligimenorrhoeic in the patient's reports. She slowly recovered but remained in a vegetative state after 3 months of neurorehabilitation. The outcome was grade 2 according to GOS.

Discussion

Pathological eating behaviour ranges from excessive to reduced appetite, dysregulation of hunger and satiation signals. The underlying cause of most of the eating disorders is a matter of controversy. As one possible epidemiological factor for self limited malnutrition we find psychological reasons with high prevalence in female teenagers, but purely psychological and psychosomatic explanations [24] have been challenged by the findings of altered serotonin and noradrenaline levels in these patients [17, 18, 23]. Arato and co-workers [1, 2] investigated hemispheric differences of the neurotransmitter distribution in post-mortem brain tissue and found higher right sided serotonin metabolite content. The imipramine binding was also higher in samples of the medial and orbital frontal regions.

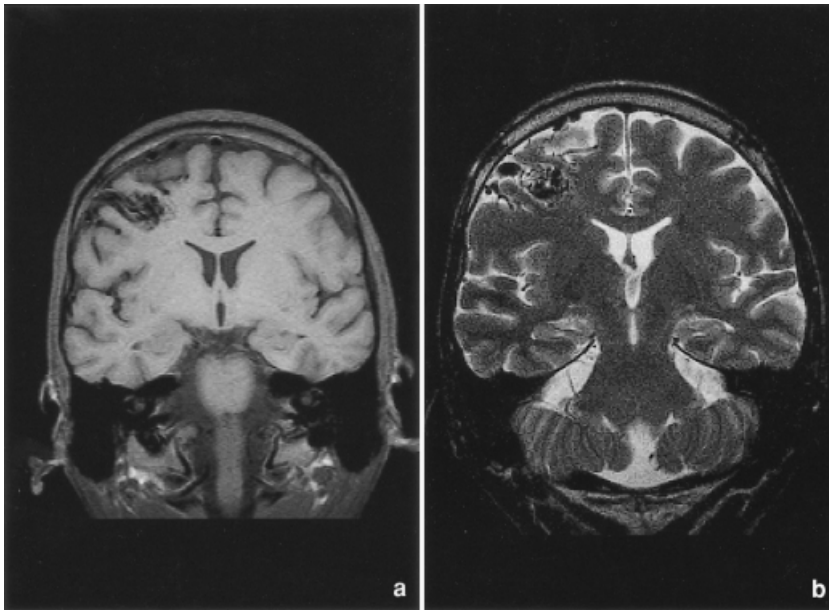


Fig. 2. Frontal arteriovenous malformation (*AVM*) in a 36-year-old man. (a) Unenhanced coronal T1-weighted MRI shows the nidus of the AVM which is supplied by branches of the right middle cerebral artery. Note also the prominent draining cortical vein. (b) Coronal T2-weighted MRI at the level of (a) demonstrates the nidus and the draining vein with flow voids. There are no signs of recent haemorrhage



Fig. 3. Frontal haemorrhage caused by a ruptured venous malformation in a 23-year-old woman. Unenhanced axial CT shows an acute right frontal haemorrhage (7 cm in maximum diameter) with surrounding oedema. Note the extensive mass effect of the lesion

These clinical and laboratory findings lead to the hypothesis of an asymmetrical distribution of the neurotransmitter system. This well balanced system could

be rendered more imbalanced by unilateral right hemispheric lesions. These findings would implicate disturbances of the neurotransmitter systems as a possible etiological factor [13, 14, 19]. However it is not clear whether these alterations are pathogenetic or epiphenomena of the diseases.

A more morphological approach to these complex diseases is the neuroradiological point of view. For eating disorders and for obsessive compulsive disorders we find cerebral changes in the MRI like atrophy or white matter changes, especially in the basal ganglia and cortico-limbic areas. This well known fact could be a consequence of malnutrition caused by food shortage as well as by selflimitation due to anorexia nervosa or bulimia on the one hand, but also be causative for the pathogenesis on the other hand [10].

A variety of eating disorders is associated with neurological diseases such as degenerative changes involving the medial temporal lobe as well as tumours involving the ventromedial hypothalamus [3, 4, 5, 15] or the temporal cortex [5], which is documented for hyperphagia, bulimia, anorexia nervosa or the so called Gourmand syndrome. This syndrome describes a preoccupation with food and fine eating and is associated with unilateral right-sided lesions involving anterior cortico-limbic structures and was first described by Regard and Landis in 1997 [22]. These data are

supported by Griffith and Hochberg [12], who found, that tumours producing anorexia were twice as often located in the right than in the left hemisphere. The anatomical studies of Cummings and Mendez in 1984 [8], Starkstein *et al.* in 1987 [25] and Regard and Landis in 1994 [21] also confirm a strong association between behavioural changes and lesions located in right frontal regions.

Other aetiological factors like strokes or encephalitis concerning temporo-mesial structures as well as severe cerebral traumas are reported for Pick disease [7].

The hypothesis of a relationship between the limbic system, especially the right frontal lobe and feeding disorders is supported by the association with seizures after severe cerebral traumas on the one hand. On the other hand this fact is proved by the so called Klüver-Bucy syndrome [9, 20], which is reported after surgical treatment for medically intractable temporal epilepsy or after severe herpes encephalitis [6]. In this special case the treatment of the seizure leads to the feeding disorder in combination with compulsive disorders.

The causative interaction of a right frontal tumour or AVM with the eating disorder in our first two cases is proved by the postoperative course. Both patients gained weight and returned to their normal occupation. There is also clear evidence of an interaction between the right frontal lesions, the limbic system, secondary generalized seizures and eating disorders as shown above.

As a conclusion we find that eating disorders like bulimia or anorexia nervosa may be associated with morphological intracerebral changes, predominantly located near the limbic system such as the ventromedial hypothalamus, mesiotemporal and temporal structures or the right frontal lobe. This also explains the possible interaction with partial seizures and is supported by laboratory findings like elevated serotonin and noradrenaline levels in the right frontal lobe.

The aetiology ranges from posttraumatic atrophy, encephalitis, bleeding from malformations or tumours to iatrogenic reasons such as microsurgical interventions for intractable epilepsy.

The excellent outcome in patient 1 and patient 2, as well as the dramatic clinical course of the young female patient is obvious.

We therefore recommend a cranial MRI for patients with eating disorders, especially in combination with atypical features like male gender or unusual early or late onset, to exclude right frontal intracerebral tumours or vascular malformations, entities, which can

easily be treated by modern microneurosurgical, radiosurgical and endovascular techniques.

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Comments

This is a well written article concerning an interesting clinical condition: anorexia nervosa. The authors had the acute insight, after treating three patients at their department for right frontal lesions, that there may be a link between right frontal lesions and severe eating disorders. Reading this paper my first impression was that the combination of the right frontal lesion and anorexia nervosa was purely a matter of chance, however, in the discussion the authors were highly successful in convincing me that it is very likely that the anorexia is caused by this right frontal lesion. Their hypothesis is very well supported by data collected from the relevant literature. The fact that the two patients who recovered well started to eat in a normal way and gained considerable weight shortly after their

treatment (where in one patient an oligo-astrocytoma grade 2 was surgically removed and in the other an AVM was obliterated by the interventional radiologist) makes their case very convincing.

C. Tulleken

This is a description of three patients with anorexia and epilepsy and a lesion in the right frontal lobe. The lesions were of a different nature – oligo-astrocytoma, AVM and a venous angioma. Location of the lesions within the frontal lobe varied greatly. The tumour (Fig. 2) is close to the frontal part of the lobe base, intracerebral haematoma of the venous malformation (Fig. 3) takes most of the frontal lobe with big mass effect and the AVM is located in the posterior and superior part of the frontal lobe, close to parietal lobe (Fig. 1). Two patients returned to normal eating habits after removal of their lesions.

I am afraid the small number of cases, diversity of lesions and their location does not justify the proposed conclusions. This does not mean that there is no relation between organic lesion of the right frontal area of the brain and anorexia nervosa, but this supposition needs more supporting observations.

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