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Creutzfeldt-Jakob disease in the psychiatric practice – case reports of the ataxic and Heidenhain variant

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Summary

Objectives. Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare fatal neurodegenerative brain disorder of variable clinical manifestation. Making right diagnosis still remains challenging. First symptoms are vague and differ between clinical subtypes of the disease. This is to present the symptoms variability and diagnostic difficulties in sCJD based on case reports of two female patients examined at time of the disease duration by psychiatrists.

Methods. Data of our patients were collected from hospital medical records.

Results. The case of patient A. P.' ataxic sCJD is an example of clinical picture suggesting neurological background of the disease almost from the symptoms' onset and being referred by psychiatrist to the neurological ward, where the right diagnosis of probable sCJD was established. In the opposite is the case of patient I. W.' Heidenhain variant of sCJD, misdiagnosed with dissociative disorder and delivering huge diagnostic difficulties, even to neurologists. In both patients the certain diagnosis was confirmed at autopsy.

Conclusions. In patients with visual disturbances of unknown etiology, even if the ophthalmological and neurological background is excluded, sCJD should be taken into consideration in the differential diagnosis.

Key words: Creutzfeldt-Jakob disease, psychiatry

Background

Creutzfeldt-Jakob disease is a fatal neurodegenerative brain disorder. Making right diagnosis remains challenging with regard to inconstant presentation and low prevalence being assessed at 1 – 1,6 : 1 000 000. The most frequent type of CJD, sporadic Creutzfeldt – Jakob (sCJD), accounts for 85-95% of all cases [1]. Moreover, the sCJD patients are a heterogeneous group divided into a few clinical subtypes which vary according to clinical manifestation, disease course and results of a diagnostic workup. World Health Organization (WHO) diagnostic criteria for sCJD are listed in Table 1[2]. A core diagnostic criterium is quickly progressing dementia but there can be seen variable psychiatric symptoms interfering clinical picture of the disease and causing misdiagnoses [3].

We describe cases of two different clinical subtypes of sCJD to emphasize inconstant clinical manifestation of the disease and diagnostic difficulties it cause. First case,

patient A.P., is a patient with ataxic type of sCJD. The clinical picture was suggestive of neurological background from the beginning and the patient was referred to neurologists by psychiatrist in outpatients. Correct diagnosis of probable sCJD was established in neurological ward and was confirmed at autopsy. The second one case is patient I.W. with rare presentation of sCJD, the Heidenhain variant. We focus mainly on this case because it delivered diagnostic difficulties and was misdiagnosed with dissociative disorder. The Heidenhain variant accounts for 3,7% of all sCJD cases [4].

Table 1. **World Health Organization diagnostic criteria for sCJD**

I Quickly progressing dementia.
IIA. Myoclonus. IIB. Visual or cerebellar disturbance. IIC. Pyramidal or extrapyramidal dysfunction. IID. Akinetic mutism.
IIIA. Typical EEG during an illness of any duration. IIIB. Positive 14-3-3 CSF assay and a clinical duration to death < 2 years. IIIC. Routine investigations should not suggest an alternative diagnosis.
Possible sCJD: I + 2/4 criteria from II + duration < 2 years.
Probable sCJD: a. I + 2/4 criteria from II + IIIA or, b. I + 2/4 criteria from II + duration < 2 years + IIIB

Case Presentation

Ataxic sCJD – patient A.P. case

A.P. was a 65 year-old woman, retired, living with husband. She was diagnosed with significant binocular myopia since she was born and she was hypertensive since few years.

Patient A.P. visited psychiatrist in outpatients because of rapidly progressing memory loss of 1 month duration. The psychiatrist noticed cerebellar gait disturbances and in the context of rapid onset of dementia and no previous psychiatric and neurological history, referred her to neurological ward for further diagnosis.

There was no meningeal signs and no focal deficits on admission to neurological ward. After one week her cerebellar gait and dementia progressed. Since the second week general muscle rigidity, total lack of communication abilities and myoclonus were noticed. In the third week more new symptoms appeared: nystagmus and akinetic mutism. Her computed tomography (CT) and magnetic resonance imaging (MRI) brain scanning showed general cortical and subcortical brain and cerebellar atrophy. Her electroencephalography (EEG) was not specific for CJD. Cerebrospinal fluid (CSF) examination excluded inflammatory process and confirmed the presence of the

14-3-3 protein. The patient fulfilled WHO diagnostic criteria for probable sCJD: the presence of progressing dementia, myoclonia, cerebellar disturbances, extrapyramidal symptoms and akinetic mutism, positive CSF immunoassay for 14-3-3 protein and the time of symptoms' duration shorter than 2 years.

Finally her general state get worse and she died in the 47th day of hospitalization because of respiratory and circulatory insufficiency.

In genetic examination no PrP gene mutations were identified. Certain sCJD diagnosis was confirmed histologically. Both histological and immunochemistry data were consistent with sCJD VV2 type according to Gambetti-Parchi classification [5].

Heidenhain variant of sCJD – patient I.W. case

I.W. was a 53 year-old woman, high school - educated, working as a count, living with husband and daughter. Her psychiatric and neurological history was silent. There was no concomitant somatic disorder. The patient died about 5 months from the onset of her visual symptoms.

The patient was first diagnosed by neurologists because of blurred vision of 1 month duration. The total time of neurological hospitalization was 10 days. The patient had word finding and articulation difficulties. She was trying to speak loud and slow to be clear for others. The electroretinography showed undisturbed retinal function; electrolyte values (sodium, potassium) were normal; MRI-angio brain scanning and ultrasonography of carotid and vertebral arteries were also normal. However single-photon emission computed tomography (SPECT) revealed diminished perfussion in postero-inferior area of the left occipital lobe and in the base of right temporal lobe (hipoccampus area). Among next days the articulation disturbances get worse and unsteady gait appeared. No clear neurological background for those disturbances was found and the decision of psychiatric and psychological consultation was made up. The patient was described as histrionic in behavior and dissimulating when asked about family relations. Moreover the patient experienced very traumatic event, her sister's death, about 5 months prior to the onset of visual symptoms. Taking into consideration all this data, the initial diagnosis of dissociative disorder was established and the patient was referred to our psychiatry ward.

Hospitalization in the psychiatry ward last for 5 days. On admission, the patient had normal autopsychic orientation but allopsychic orientation was disturbed. No hallucinations and delusions were present. She was tearfulness and of labile mood. The patient was able to walk only with help. She was answering with single words or sounds. Neurological examination revealed increased muscle tension in lower and upper limbs. Her psychomotor drive was temporary accelerated: she was loud, with sleep disturbances. Her treatment consisted of: clorazepate ad hoc (maksimum dose - 100 mg/day), sulpiride (only during 2 first days; maksimum dose - 200mg/day), doxepin (during all 5 days; maksimum dose – 100mg/day). On the third day of hospitalization her general state declined: she lost her communication abilities (akinetic mutism), she was spitting out medicines and food, progressive worsening of quantitative disturbances in conscious was noted and nuchal rigidity appeared. During fourth and fifth day the

body temperature was elevated till 37 – 38°C which was accompanied by elevated white blood count (WBC) (11,3 K/µl) and slightly elevated potassium concentration (5,04 mmol/l). A lumbar puncture was done to exclude neuroinfection. CSF examination excluded inflammatory process. There was no examination towards 14-3-3 protein presence because there was no CJD suspicion. EEG was not done because patient was too unwell for hospital transfer. On the fifth day of hospitalization the patient fell into coma. The nuchal rigidity was still present. The Babinski sign was negative.

The patient was transferred to the intensive care unit with a suspicion of neuroleptic malignant syndrome. She died in about 3 months because of respiratory and circulatory insufficiency.

The right diagnosis was pathologically established at postmortem examination. We can see that she fulfilled WHO diagnostic criteria for possible sCJD because of quickly progressing dementia, visual and cerebellar disturbance, extrapyramidal dysfunctions, akinetic mutism. It is possible that she fulfilled also WHO diagnostic criteria for probable sCJD. However because of above listed reasons, EEG and 14-3-3 CSF assay examination was not done.

Discussion

World Health Organization diagnostic criteria for possible and probable sCJD are shown in Table 1 [2]. Certain diagnosis of sCJD can be established pathologically at postmortem examination. Characteristics of sCJD may be vague at onset and inconstant during the course. The WHO core diagnostic criterium is quickly progressing dementia. Other symptoms which may appear are: cerebellar ataxia, myoclonus, seizures, limb paresis. Visual symptoms developed during sCJD course can be of blurred vision, visual field defect, optical hallucinations, and even cortical blindness. They are frequent [5] and listed between WHO diagnostic criteria [2]. They can lead to misdiagnoses while isolated, existing without concomitant neurological symptoms suggestive of sCJD, ie, myoclonia, pyramidal and extrapyramidal symptoms. Few weeks visual symptoms isolation is the main characteristic of the Heidenhain variant. Cognitive decline is unanticipated and quickly progressing.

Cooper et al. [4] analysed 594 sCJD patients and concluded that it affects people aged from 50 to 88 years which resembles our cases. Patient A.P. was 65 and patient I.W. was 53 years old. sCJD in general leads to death in few months [6]. Patient A.P. died after 2,5 month from the symptom onset, I.W. – after 5 months. The shorter time of duration was seen in the older patient (patient A.P.). However it can not be concluded that the older patient is the more aggressive is the disease course. Unusually long survival (over 2 years) was described as well, both in 37 year-old women [7] and 77 year-old women [8]. Unfortunately only in one patient, A.P., a genetic assessment of valine/methionine (M/V) polymorphism at *PrPc* 129 codon was done. It is reported that homozygotes VV and MM are more susceptible and heterozygotes VM are more resistant to developing sCJD [9]. All Heidenhain variant cases reviewed by Cooper et al. [4] were homozygotes MM. In patient A.P. case, both histological and immunohistochemistry data were consistent with sCJD VV2 of the Gambetti-Parchi classification

[5]. Periodic sharp waves complexes (PSWCs) in EEG or a detection of 14-3-3 protein in CSF may be suggestive but not pathognomonic of sCJD. EEG with PSWCs can be also seen in Alzheimer's Disease and Dementia with Lewy Bodies [10, 11]. Moreover PSWCs can be seen at any time of duration of the sCJD, not necessarily from the beginning. In I.W. case, EEG was not registered because of patient's bad condition. Patient A.P.' EEG was not specific of sCJD. The 14-3-3 CSF assay examination in patient A.P. was positive. It is noteworthy that this examination can give false positives in hypoxic and metabolic encephalopathies and in cases of cerebral metastases and herpes simplex encephalitis [12,13].

In reviewed articles SPECT in sCJD revealed diminished blood perfusion in the frontal, temporal, parietal and occipital lobe [14]. SPECT was done in patient I.W. and revealed diminished perfussion in postero-inferior area of the left occipital lobe and in the base of right temporal lobe (hipoccampus area). Neurologists after taking into consideration all diagnostic workup results excluded neurological background for patient's visual symptoms. Magnetic resonance imaging done in patient I.W. at the time of visual symptoms isolation was normal and was not repeated. MRI and CT brain scanning made in patient A.P. after one month from the symptom onset revealed brain and cerebellar atrophy. Weber-Donat et al. [15] reported one Heidenhain variant case and emphasized that MRI must be repeated in patients with visual symptoms of unknown etiology. MRI can be false negative when visual symptoms are isolated. In reported by Weber-Donat et al. [15] case MRI showed cortical and basal ganglia hyperintensities, when a constellation of neurological symptoms appeared and EEG became typical of sCJD. It is noteworthy that in sCJD many psychopathological symptoms can appear and they may be misdiagnosed with psychiatric disorders. Yen i wsp. [3] reviewed 8 cases of confirmed sCJD, hospitalized in neurological ward during the last 15 years and indicated that 5 of them had psychiatric symptoms: disturbances in mood, thoughts, behavior, perception and were misdiagnosed with psychiatric disorders, one underwent electroconvulsive therapy, another one was diagnosed with neuroleptic malignant syndrome. The authors concluded that it happens when psychiatrists examine patient with sCJD at the beginning of the disorder. However patient I.W. was first assessed by neurologists and ophthalmologists and referred by them to the psychiatric ward after they excluded structural background for patient's symptoms. Additionally misleading data were of patient's sister death previous to visual symptoms onset. Wall et al. [16] reviewed 126 sCJD cases and confirmed the presence of psychopathologic symptoms: depression, anxiety, psychosis, disturbances in behavior, sleep disturbances in 80% of patients during the first 100 days of disease duration and in 26% of them they were initial symptoms.

Conclusions

In patients with visual disturbances of unknown etiology, even if the ophthalmological and neurological background is excluded, sporadic Creutzfeldt-Jakob disease should be taken into consideration in the differential diagnosis.

Болезнь Крейтцфелдта-Якоба в психиатрической практике. Описание наблюдений атактической формы и Хейденхаина

Содержание

Задание. Спорадически встречаемая болезнь Крейцфелдта-Якоба (БКЯ) является редкой смертельной йейродегенеративной болезнью мозга с неопределенной клинической картиной. Ее правильный диагноз до сих пор является редкостью. Начальные симптомы неопределенны и отличаются между выделенными клиническими формами БКЯ. Заданием работы является представление разнородности симптомов и диагностических трудностей на основании описания наблюдений двух пациентов обследованных психиатрами на определенном этапе болезни.

Метод. Описание наблюдений были разработаны на основе доступной документации медицинских данных.

Результаты. Наблюдение атактичной формы БКЯ пациентки А.П. является примером клинической репрезентации БКЯ, указывающее на нейрологический фон болезни уже в начале появившихся симптомов и правильно оцененных психиатром с направлением больной в неврологическое отделение. В отделении диагностирована возможная болезнь БКЯ. Контрастом является вариант Хенденхаина пациентки И.В., неправильно распознанный как диссоциацийное нарушение, известное из литературных данных из трудностей диагностического порядка, даже неврологам. У обеих женщин диагноз БКЯ подтвержден секционном исследованием.

Выводы. Во всех случаях зрительных симптомов с неясной этиологией, даже если вначале исключается нейрологический фон и изменения глазного заболевания, БКЯ должна приниматься во внимание при дифференциальной диагностике.

Ключевые слова: болезнь Крейтцфелдта-Якоба, психиатрия

Creutzfeldt-Jakob-Krankheit in psychiatrischer Praxis – Fallbeschreibung: Ataxie und Heidenhain-Variante

Zusammenfassung

Ziel. Sporadische Creutzfeldt-Jakob-Krankheit (sCJK) ist eine sehr selten auftretende tödlich verlaufende spongiforme Enzephalopathie mit nicht fixem klinischen Bild. Ihre richtige Diagnosestellung ist immer noch eine Herausforderung. Die Krankheitssymptome sind am Anfang unklar und unterscheiden sich zwischen den ausgesonderten klinischen Typen von sCJK. Das Ziel der Studie ist die Besprechung der Unterschiedlichkeit der Symptome und der diagnostischen Probleme in sCJK aufgrund von zwei Fällen, zwei Patientinnen, die durch die Psychiater auf einer Etappe der Krankheit untersucht werden.

Methode. Die Fallbeschreibungen wurden aufgrund der zugänglichen medizinischen Dokumentation bearbeitet.

Ergebnisse. Der Fall einer Ataxie bei sCJK der Patientin A.P. ist ein Beispiel für die klinische Darstellung von sCJK, das den neurologischen Hintergrund der Krankheit schon beim Auftreten der ersten Symptome vermuten lässt. Die Patientin wurde richtig vom Arzt in die neurologische Abteilung eingewiesen, wo die Diagnose einer wahrscheinlichen sCJK gestellt wurde. Im Gegensatz dazu steht die Heidenhain - Variante der Patientin I.W., die nicht korrekt als für die diagnostische Problematik von der Literatur bekannte dissoziative Störung diagnostiziert wurde. Bei den beiden Frauen wurde die Diagnose sCJK in der Autopsie bestätigt.

Schlussfolgerungen. In allen Fällen, wo optische Symptome von unbekannter Ätiologie auftreten, auch wenn am Anfang der neurologische Hintergrund ausgeschlossen wurde, sollte sCJK bei der Differentialdiagnostik in Erwägung genommen werden.

Schlüsselwörter: Creutzfeldt-Jakob-Krankheit, Psychiatrie

La maladie de Creutzfeldt-Jakob dans la pratique psychiatrique – description des variantes : ataxique et d' Heidenhain

Résumé

Objectif. La maladie de Creutzfeldt-Jakob (MCJ) sporadique est une maladie mortelle rare, maladie nuerodégénérative du cerveau, dont l'image clinique est instable. Son diagnostic juste reste toujours difficile. Ses premiers symptômes sont vagues et ils diffèrent dans les variantes cliniques particulières de MCJ. Ce travail veut présenter cette diversité des symptômes et les difficultés diagnostiques de MCJ en décrivant deux cas de patientes examinées par les psychiatres dans un moment donné de leurs maladies.

Méthodes. On analyse la documentation médicale de deux patientes.

Résultats. Le cas de la patiente A.P. est un exemple de la variante clinique de MCJ sporadique qui suggère le fondement neurologique déjà au début des symptômes, la patiente est bien diagnostiquée à l'hôpital neurologique (diagnose- probable MCJ). Le deuxième cas de la patiente I.W. est différent. Son diagnostic est erroné : troubles dissociatifs, troubles difficiles à diagnostiquer même pour les neurologues, tendis qu'elle souffre de la variante d'Heidenhain de MCJ. Les deux diagnostics de ces femmes sont confirmés par leur autopsie.

Conclusions. Dans tous les cas des troubles visuels dont l'étiologie est incertaine, même si l'on exclue le fond neurologique et ophtalmologique, il faut prendre en considération MCJ comme possibilité diagnostique.

Mots clés : maladie de Creutzfeldt-Jakob, psychiatrie

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