Tuberous sclerosis epilepsy and psychosis by adults

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Introduction

The tuberous sclerosis (TS) or tuberous sclerosis complex (TSC) is a multisystem, autosomal dominant disorder by children and adults, results from mutations in one of two genes, TSC1 (encoding hamartin) or TSC2 (encoding tuberin). First described in depth by Bourneville in 1880 (Morbus Bourneville, Epiloa) [1].

TS and TSC often causes disabling neuropsychiatric disorders, including epilepsy, mental retardation, autism and psychosis.

Additional major features of the disease include dermatologic manifestations such as facial angiofibromas, renal angiomyolipomas, and pulmonary lymphangiomyomatosis. TSC has a wide clinical spectrum of disease, and many patients have minimal signs and symptoms with or without neurologic and psychiatric disability [2].

TS is once of “phakomatosis” a group of congenital hereditary developmental anomalies having selective involvement of tissues of ectodermal origin, which develop disseminated glial hamartomas. Examples of phakomatosis are neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, and von Hippel-Lindau disease” [3].

The clinical diagnostic criterias are divided in two groups:

1. Major criterias (facial angiofibroma, ungual fibroma, shagreen patch, hypomelanotic macula, cortical tuber, subependymal nodules, subependymal giant-cell tumor, retinal hamartoma, cardiac rhabdomyoma, renal angiomyolipoma, lymphangiomatosis), and

2. Minor criterias (multiple pints in dental enamel, hamartomatas rectal polyps, bone cysts, cerebral white-matter radial migration lines, gingival fibromas, retinal acromic patch, “confetti” skin lesions - groups of small lightly pigmented spots, multiple renal cysts). The diagnosis is fulfilled with two major features, or one major feature plus two minor features [4]. Age of onset of some typical lesions is in fetal life (cortical tuber, cardiac rhabdomyoma), in infancy (ungual fibroma, hypomelanotic macula, retinal hamartroma, facial angiofibroma), in adolescence (shagreen patch, subependimal nodules, lymphangiomyomatosis) and in adulthood (renal angiomyolipoma).

The molecular genetics analysis in multigenerational families and positional cloning were used to map both the TSC1 and TSC2 genes 32-34. The TSC2 gene, which is located on chromosome 16p13, encodes a transcript of 5.5 kb containing 41 exons and encompassing 40 kb of genomic DNA; there are several alternatively spliced versions [5]. The TSC1 gene, which is located on chromosome 9q34, encodes a transcript of 8.6 kb, containing 23 exons and encompassing 55 kb of genomic DNA [6,7]. It is the possibility to prevention of disease with cordocentesis and genetic analysis in first 3 months of pregnancy.

By 5 patients (3 M, 2 F, average age 35, 7 years, from different part of former Yugoslavia, mostly South Serbia)A , was admitted between 2013 and 2016 to University Clinic of Psychiatry in Belgrade (Serbia). Most (4 from 5) developed paranoid psychotic episodes 1 to 2 years prior to admission, epileptic seizures partialy and generalized (3 from 5), anxiety, disorders and depression. Most (4 from 5) was treated as with flufenazine 5 mg per diem and chlorpromazine 25 mg (3x1), once patient was treated with haloperidol (5 mg pro die), and all 5 patients with seizures with carbamazepine (3x200 mg) and phenobarbital (50-100 mg in the evening).

Referred to our clinic in 2007. and admitted first time to a complete neuropsychiatric exploration, because of increased frequency of seizures, hypertensive crisis, depression, worrying about work, paranoid psychotic elaboration.

In family history - bz all patients evidence of skin lesions. In physical examination in somatic findings the patients were afébrile, eupnoic, hypertensive 155/100 mm Hg to 180/110 mm Hg, cardiopulmonally compensated. All have multiple red papules on facial skin, 3 patients larger angiofibroma in left frontal or parietal regions, multiple hypomelanic maculas on body and Shagrin patches on body skin.
Psychiatric examination revealed discretely slowed flow of thinking, mild mental retardation and unsistematized persecutory delusions.

In neurological status - 4 patients have daily 1-2 epileptic seizures (partial and partial with secondary generalization).

During clinical examination additional diagnostic procedures were done.

The typical EEG was hypersynchronous, alpha-theta type, with single irritative bitemporal changes, more on the right or left side.

Endocranial CT showed periventricular calcifications suggesting probably TS. Endocranial MRI - cortico-subcortical and subependymal nodular lesions typical for Tuberous Sclerosis (TS).

Liver (Ultra Sound): multiple hiperehogenous changes, one susp. haemangioma. Kidney (Ultra Sound): Left or right kidneys - hypoechogenous nodules, many smaller, 5-6 cysts and calcificates, bzy all patients. Neuropsychological examinations (interview, VITI, TMT A, B; RAVLT, RCF, FF, KF, Rch): MMSE average 23/30, IQ average 70, showed: mild retardet, introverted and anxious personality, with tendencies to paranoid elaboration. The cognitive and affective changes by all patients were organic origin.

Discussion

Chronology of illness: epileptic seizures, typical skin lesions (facial angiofibroma, shagreen patch), psychotic disorder (paranoid psychosis) and arterial hypertension (kidney origin) fulfilled all diagnostic criteria for Tuberous sclerosis: typical lesions of CNS (cortico-subcortical and subependymal nodular lesions), skin lesion, liver and kidneys nodules and cystes.

The patients were successfully treated wit symptomatic therapy: neuroleptica (antipsychotica), antiepileptica and antihypertensive drugs/diuretica (flufenazine, 2,5 mg, carbamazepine, 400 mg, phenobarbitone, 100 mg, diazepam, 10 mg, hydrochlorothiazide, 1 tab. on second day.

The results were reduced paranoid delusions and reduced frequency of seizures, reduced arterial hypertension.

Conclusions

According to the clinical presentation (epilepsy, mental retardation, multiple typical dermatological signs) and discovered pathognomonic multisystemic changes (cortical and subcortical tubers, subependymal nodules, kidney and liver nodules and cysts), we must think about phacomatosisi and in most cases conclude that the diagnosis is Tuberous sclerosis.

Paranoid psychotic disorder by patient with symptomatic epilepsy (organic substrate + vulnerable personality) made this case even more complex, but due to psychiatric symptoms and epilepsy (as a starting point), we were able to initiate our search for etiology of the disorder and to go retrogradely to the cause.

Tuberous sclerosis is very important in differential diagnosis of many multisystemic disorders.

References

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