Neurological and immunological phenotypes in Ataxia Telangiectasia

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Ataxia-telangiectasia (A-T) is an autosomal recessive, multisystem neurodegenerative disorder of significant social and global burden.

The incidence is 1:40.000-100.000.

Although AT is considered an immunodeficiency, the initial symptoms are usually neurological. Some patients have no significant immune dysfunction despite advanced disease.

It is critical to address the disease's specific symptoms and prevent complications.

OBJECTIVE

Clinical and laboratory findings in comprehensive multidisciplinary evaluation

PATIENTS

<18 years old diagnosed with A-T, date 2005 -2021

METHODS

AT-NEST (A-T Neuro Examination Scale Toolkit)

SARA (Scale for Assessment-Rating of Ataxia), ICARS (International Cooperative Ataxia Rating Scale)

Denver II developmental test, Turkish Standardization and Adaptation

Structured clinical evaluation

Immunological tests

Speech and language tests

RESULTS

N=39 patients
F/M=21/18
Age 26-232, median 6.9 years
Age at diagnosis median 33 (6-108) months
Age at first symptoms: median 5 (3-77) months
Age at first neurological symptoms median 9 (3-77) months

Initial symptoms:
"trunk swaying" when sitting without support 12 (30.8%)
unsteady gait when started walking 11 (28.2%)
Recurrent infections 7 (17.9%)
Drooling 28/39 (71.8%)

Signs:

Weight <3rd percentile 14/39 (35.9%)

Scleral telangiectasia: 28/39 (71.8%)

5/9 without telangiectasia were >60 months old

Cerebellar (ataxia, dysarthria) : 38/39 (97.4%)

Four patients <3 years old had mild symptoms: unsteady gait, "trunk swaying", retrocollic jerk

Eye movements:

Oculomotor apraxia, delayed saccade latency: 20/39.

limitation of upward gaze 15/39

Extrapyramidal findings:

dystonia 18 (46.1%)

choreiform movements 15 (38.5%)

dystonic tremor: 2 patients

negative myoclonia: 2 patients.

bradykinesia: 30/39 (76.9%)

Other findings:

Peripheral neuropathy: 6 patients

Comorbid disease: Leukemia, Hodgkin lymphoma, autoimmune hemolytic anemia, early puberty, asthma (n=1 each)

Cognitive assessment :

normal 13/20 (65%)

mild/moderate impairment 7/20 (35%)

Speech and language:

speech sound disorder 15/22 (68.2%)
language disorder 4/9 (44.4%)
Impaired response time: 23/39 (59%)
Intelligibility in context scale score: median 23.5 (max.35)

Phenotype varied between patients with same genetic mutation at similar ages.

MRI:

Cerebellar atrophy in 12/26 (46.1%)
(diffuse; n=7, folial; n=4, vermian; n=1)

Immunological tests:

Normal: 2/37 (5.4%)
Low serum Ig levels 32/37 (86.5%)
Lymphopenia 30/37 (81.1%)
Abnormality in lymphocyte subsets 28/32 (87.5%)
Serum alphafetoprotein elevated 38/38 (100%)

TREATMENT

Immunoglobulin G iv 10/37 (27%)

CONCLUSION

AT should be considered in patients with neurological symptoms only.

Follow-up studies allow documentation of:

- phenotypic diversity including patients with same genetic mutation at similar age early findings natural history of the disorder.