Purkinje cell cytoplasmic antibody type 1 (PCA-1)–IgG (or anti-Yo) is characteristically detected in women with gynecological or breast adenocarcinoma. We describe 2 unique scenarios occurring in 1 patient: PCA-1 paraneoplastic autoimmunity in a child, and a paraneoplastic neurological disorder in the context of Down syndrome.

Observations

A child with Down syndrome and a history of adrenocortical carcinoma resected at age 1 year presented at age 7 years with cerebellar ataxia of subacute onset. Paraneoplastic serological and cerebrospinal fluid evaluations revealed PCA-1. Serological and biochemical studies also supported a diagnosis of subclinical autoimmune hypothyroidism. Extensive serum, urine, and radiological testing did not reveal a new or recurrent neoplasm. Neurological improvements after standard immunotherapy were lacking.

Conclusions and Relevance

Solid organ neoplasms are uncommon among patients with Down syndrome, but organ-specific autoimmune diseases are common. In our patient, Down syndrome–related impaired T regulatory lymphocyte function (previously reported) may have resulted in both enhanced immunity against an undetected solid neoplasm and paraneoplastic neurological (PCA-1) autoimmunity.
and oral prednisone taper. Venous immunoglobulin, intravenous methylprednisolone, motor disorder did not improve despite treatment with intra-cult neoplasm was not undertaken. Exploratory surgery for oc-tigraphy findings were all normal. Exploratory surgery for oc-
graphic findings, and metaiodobenzylguanidine-based scin-
tigraphy was also noted (0.15 nmol/L by radioimmunoprecipi-
tation assay; reference range, <0.03 nmol/L). There was no
IgG also was detected at 1:2]) (Figure). Glutamic acid decarboxylase 65 (GAD65)–
detected at 1:2]) (Figure). These findings were confirmed by
Western blot (Figure). Glutamic acid decarboxylase 65 (GAD65)-
IgG also was detected (0.15 nmol/L by radioimmunoprecipi-
tation assay; reference range, <0.03 nmol/L). There was no
biochemical or imaging evidence of neoplasia: urinary vanil-
lymandelic acid and homovanillic acid levels, whole-body
magnetic resonance imaging and positron emission tomo-
graphic findings, and metaiodobenzylguanidine-based scint-
tigraphy findings were all normal. Exploratory surgery for oc-

thibrosis was not undertaken. The risk of acute leukemias is recognized to be increased
10- to 20-fold in patients with Down syndrome (susceptibility
genes are located in the long arm of chromosome 21), but the
risk of solid neoplasms is reported to be reduced. In con-
trast, this child had adrenal carcinoma (not previously re-
ported with PCA-1) 5 years before neurological symptom on-
set and had a family history of solid neoplasms. Although no
neoplasm was detected at the time of neurological presenta-
tion, it is possible that she had an occult reoccurrence of the
adrenal carcinoma or had a new occult gynecological or breast
adenocarcinoma. As well as having an unusually high risk for solid neo-
plasm, this patient also had an abnormal immunological back-
ground. Several autoimmune diseases (eg, celiac disease, thy-
roid disorders, and type 1 diabetes mellitus) are reported
disproportionately in patients with Down syndrome, and in-
deeped patient was additionally seropositive for thyroid an-
tibodies and GAD65-IgG. The detection of GAD65-IgG (0.15
nmol/L) and thyroid autoantibodies was consistent with a pre-
disposition to organ-specific nonneurological autoimmunity
(including thyroid disease, type 1 diabetes mellitus, and per-
nicious anemia) rather than neurological disease. Levels of
GAD65-IgG in patients with nonparaneoplastic autoimmune
neurological disorders usually exceed 20 nmol/L.

The thymus glands of infants with Down syndrome are ar-
chitecturally and functionally abnormal and exhibit im-
paired T-lymphocyte maturation. It is further reported that
natural (thymic) T regulatory lymphocytes in patients with
Down syndrome have reduced suppressive activity against au-
toreactive T lymphocytes. We therefore speculate that in our
patient, impaired T regulatory lymphocyte function may have
resulted in both enhanced immunity against an undetected
solid neoplasm, either recurrent or new, and paraneoplastic
neurological (PCA-1) autoimmunity. It is also plausible that this
child’s personal and family history of solid neoplasms and her

Discussion
To our knowledge, the occurrence of a paraneoplastic neuro-
logical disorder in a patient with Down syndrome as well as the
pediatric age of this PCA-1–IgG-positive case are both unique
observations in the literature. The patient presented with cer-
ebellar ataxia, which did not improve with immunotherapy,
as is typical of PCA-1 autoimmunity in which histological and
in vitro immunological studies have demonstrated early
neuronal loss mediated by cytotoxic CD8+ T lymphocytes. Auto-
tibodies specific for intracellular antigens generally lack
pathogenicity for intact cells.
earlier documented precocious puberty may have promoted development of an occult müllerian or breast adenocarcinoma. In this immunological, genetic, and hormonal context, a dysregulated cdr2-specific immune response may have restrained the growth of an adenocarcinoma at the expense of neurological autoimmunity.

REFERENCES