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A 39-YEAR-OLD FATHER IS DIAGNOSED IN ADULTHOOD AS HAVING PARTIAL DIGEORGE ANOMALY WITH A COMBINED T- AND B-CELL IMMUNODEFICIENCY AFTER DIAGNOSIS OF THE CONDITION IN HIS DAUGHTER

We describe an adult with partial DiGeorge anomaly (DGA), whose features were first noted after diagnosis of the condition in his daughter. DGA is associated with immunodeficiency, hypoparathyroidism, conotruncal cardiac defects, and characteristic facial features.¹ Most DGA cases have a microdeletion of chromosome 22q11.2, occurring sporadically. However, in 10% to 20% of cases, it is inherited in an autosomal dominant pattern.² Our case is unique because of the patient's diagnosis of DGA in adulthood after that of his daughter and his unusual combined immunodeficiency.

Our patient is a 39-year-old, white man with a history of recurrent sinopulmonary infections, otitis media, and mastoiditis requiring mastoidectomy. The DGA features found in this patient include a T- and B-cell immunodeficiency, a heterozygous 22q11.2 deletion, hypoplastic ear cartilage, mild cognitive delays, and a daughter with typical DGA. Although he has no history of hypocalcemia, he had a low parathyroid hormone level of 8 pg/mL (10–65). His echocardiogram showed no cardiac defect.

His daughter presented with typical partial DGA at 1 month of age with hypocalcemic seizures, hypoparathyroidism, and an atrial septal defect. She also had a heterozygous 22q11.2 deletion. Immune studies showed decreased immunoglobulin levels that normalized by 3 years of age. She had persistently low antibody responses to *Streptococcus pneumoniae*. Percentages of CD3⁺ and CD4⁺ T cells were low, but her T-cell function was normal. She had a history of recurrent otitis media, which improved after myringotomy

tube placement. She currently has infrequent infections without prophylactic treatment.

Her father was evaluated for DGA because of his daughter's diagnosis, his history of recurrent infections, and facial dysmorphic features. His immune workup revealed profoundly impaired T-cell immunity as summarized in Table 1. His absolute lymphocyte count and absolute CD3⁺ T-cell count ranged from low to midnormal (824 to 2,238 and 610 to 1,522 cells/mm³, respectively). His naïve T-cell count and CD4⁺CD45RA⁺ and CD4⁺CD45RA⁺CD62L⁺ cell count were decreased to 14% to 15% and 2% of the CD4⁺ T-cell count compared with 33% to 66% and 59% of the CD4⁺

Table 1. Immunologic Studies in an Adult Patient With Partial DiGeorge Anomaly

Study	Finding	Reference range
Lymphocytes, /mm ³	824–2,238	1,400–3,300
CD3 ⁺ , %	68–74	54–94
CD3 ⁺ , /mm ³	610–1,522	1,000–2,200
CD4 ⁺ , %	43–51	40–56
CD4 ⁺ , /mm ³	912–962	530–1,300
CD8 ⁺ , %	20–25	17–45
CD8 ⁺ , /mm ³	358–560	330–920
CD20 ⁺ , %	17–18	7–17
CD20 ⁺ , /mm ³	380–403	50–390
CD56 ⁺ , %	8–9	6–26
CD56 ⁺ , /mm ³	143–201	70–480
CD4 ⁺ CD45RA ⁺ , %	14, 15	33–66
CD4 ⁺ CD45RA ⁺ CD62L ⁺ , %	2	59
CD8 ⁺ CD45RA ⁺ CD62L ⁺ , %	15	28
CD8 ⁺ CD45RA ⁺ , %	65	61–91
CD19 ⁺ CD27 ⁺ , %	65, 37	>10
PHA, %NR	6.7	>50
Concanavalin A, %NR	2.5	>50
PWM, %NR	2.7	>50
<i>Candida albicans</i> , SI	0.7	>3
Tetanus toxoid, SI	1.1	>3
Allogeneic B cells, SI	1.7	>3
IgG, mg/dL	91–96	639–1,349
IgM, mg/dL	34–57	56–352
IgA, mg/dL	<6.7	70–312
IgE, IU/mL	<2	1.53–114
IgG1, mg/dL	68	280–1,020
IgG2, mg/dL	<17	60–790
IgG3, mg/dL	20	14–240
IgG4, mg/dL	<0.2	11–330
Anti-A	4	≥16
Anti-B	2	≥8
Antidiphtheria toxoid, μ g/mL	0.01	≥0.01
Antitetanus toxoid, μ g/mL	<0.10	≥0.15
Postvaccination	All 12 serotypes	≥2.0
anti- <i>Streptococcus pneumoniae</i> , μ g/mL	<0.6	

Abbreviations: PHA, phytohemagglutinin; PWM, pokeweed mitogen; MLC, mixed lymphocyte culture to B-cell alloantigens; %NR, percentage of normal response; SI, stimulation index.

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T-cell count, respectively, in simultaneous healthy controls. He was anergic to *Candida albicans* and tetanus toxoid by delayed-type hypersensitivity testing. Lymphoproliferative responses were markedly decreased to mitogens, antigens, and alloantigens.

His B-cell workup revealed low IgG (91 to 96 mg/dL), IgA (<6.7 mg/mL), and IgM (34 to 57 mg/dL) levels. Antibody responses to polysaccharide antigens (*S pneumoniae*), protein antigens (diphtheria and tetanus toxoids), and isohemagglutinins were all decreased. He did not respond to polysaccharide pneumococcal immunization.

Prophylactic trimethoprim-sulfamethoxazole treatment was discontinued secondary to Stevens-Johnson syndrome. Monthly intravenous immunoglobulin infusions markedly decreased his respiratory infections. Malaise before infusions prompted a switch to subcutaneous gammaglobulin infusions, which improved this symptom.

Although our patient does not have cardiac defects associated with DGA, he meets the criteria for partial DGA with a combined immune defect, recurrent infections, facial dysmorphic features, and the 22q11.2 microdeletion.^{3,4} Other findings that support this diagnosis include his low parathyroid hormone level and his daughter's definitive DGA diagnosis. The clinical spectrum of patients with this microdeletion includes those without the full DGA phenotype.⁴ Although cardiac abnormalities and hypocalcemia are frequently seen in patients with DGA, the frequency of these findings is 49% to 83% and 17% to 60%, respectively.⁴

Approximately 80% of patients with DGA have immune abnormalities, which are diverse.⁵ The most common immune abnormality in DGA is a T-cell cytopenia due to hypoplasia of the thymus, followed by impaired T-cell function and humoral deficiencies.⁵ Chinen et al⁶ found that T-cell numbers in DGA decrease over time, which may be due to involution of the thymus. In patients with 22q11.2 microdeletion and partial thymic hypoplasia, decreased lymphoproliferative responses to *C albicans* and tetanus toxoid but not phytohemagglutinin and diphtheria toxoid have been observed.⁷

Humoral abnormalities are observed in 15% of patients with DGA.⁵ Immunoglobulin levels in patients with DGA are typically normal, but hypogammaglobulinemia has been reported.⁸ Functional antibody deficiencies may occur, especially selective antibody deficiency to polysaccharide antigens.⁸ Recurrent sinopulmonary bacterial infections due to antibody defects are common in patients with DGA.

Our patient with partial DGA diagnosed in adulthood reveals profoundly impaired T-cell function as demonstrated by T-cell lymphopenia secondary to impaired thymopoiesis, markedly decreased T-cell responses to mitogens and recall antigens, and profound hypogammaglobulinemia. These immune abnormalities may have progressed with age, secondary to involution of some thymic tissue he had earlier in life. Parents of children with DGA who have clinical features of

DGA themselves should be evaluated for DGA with a comprehensive cellular and humoral immune evaluation. This case also illustrates that the 22q11.2 microdeletion may present with variable immunologic and clinical features, even in inherited cases.

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SEVERE GENERALIZED EXANTHEMA DUE TO ETANERCEPT GIVEN FOR SEVERE PLAQUE PSORIASIS

Etanercept is a recombinant dimeric fusion protein consisting of a tumor necrosis factor α (TNF- α) receptor ligand-binding region linked to the Fc portion of human IgG1. The most common adverse effects are mild injection site reactions, upper respiratory tract infections, headaches, and rhinitis.¹

A 50-year-old woman with severe psoriasis was treated with etanercept for 3 months, providing clinical benefit without adverse effects. One year later, she reinitiated etanercept therapy (25-mg subcutaneous injections twice weekly) owing to a relapse of psoriasis. Two hours after receiving dose 12

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