

A Rare Case of Co-occurring Fanconi Anemia and Primary Ciliary Dyskinesia

Eş Zamanlı Fanconi Anemisi ve Primer Silyer Diskinezili Nadir Bir Olgu

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To the Editor,

A 7-year-old boy was referred to the hematology clinic for persistent thrombocytopenia detected during an infection. The patient had frequent bronchiolitis attacks during the first 3-4 years of life and was later evaluated for chronic productive cough. Sweat chloride testing for cystic fibrosis was normal and no pathogenic variant was detected in cystic fibrosis-related genetic analysis. The family reported no pneumonia diagnosis but noted recurrent productive cough. He also experienced recurrent sinusitis, and chest computed tomography showed widespread bronchiectasis, predominantly in the lower lobes. His history included neonatal surgery for duodenal atresia. The parents were consanguineous. No family history of infertility or hearing loss was reported, though a sibling had renal malposition. Physical examination revealed a height standard deviation score (SDS) of -1.6, weight SDS of -2.45, and body mass index SDS of -2.79. Dysmorphic facial features, microphthalmia, low-set ears, widespread hypermelanotic macules, ecchymoses, carious teeth, and inguinal lymphadenopathy were noted. Blood count analyses revealed hemoglobin of 10.3 g/dL, mean corpuscular volume of 93 fL, leukocyte count of $3.5 \times 10^9/L$, and platelet count of $97 \times 10^9/L$. At presentation, cytopenias were mild and the patient did not require red blood cell or platelet transfusion support. Bone marrow aspiration and biopsy showed hypoplastic marrow with 15% cellularity without dysplasia. Although cytopenias were mild at presentation and no transfusion support was required, hematopoietic stem cell transplantation (HSCT) was indicated due to the diagnosis of Fanconi anemia with significant bone marrow hypocellularity and the progressive nature of the disease, in the presence of a human leukocyte antigen (HLA)-identical sibling donor. A chromosomal breakage test performed with diepoxybutane was consistent with Fanconi aplastic anemia (FAA). FAA is among

the most common inherited bone marrow failure syndromes of childhood, characterized by progressive cytopenias and predisposition to malignancy [1]. Using whole-exome sequencing, we identified a rare, likely pathogenic intragenic deletion variant, *FANCA*: NC_000016.10 (NM_000135.4): c.(1470+4_1473)_(1900+1_1901-1)del, resulting in the deletion of exons 16-21 of the gene. Additionally the patient had a homozygous, likely pathogenic frameshift variant in the *TTC12* gene, NM_017868.4: c.1516del, p.(Leu506CysfsTer16), which is expected to result in nonsense-mediated decay. No additional primary ciliary dyskinesia (PCD)-specific diagnostic tests, such as nasal nitric oxide measurement, high-speed video microscopy, or transmission electron microscopy, were not available. The diagnosis of PCD was established based on the presence of a homozygous pathogenic *TTC12* variant together with a compatible clinical phenotype, in accordance with current genotype-supported diagnostic frameworks. The results were confirmed by gap-polymerase chain reaction and next-generation sequencing-based targeted variant analyses. Segregation analysis confirmed parental carrier status, consistent with consanguinity. *TTC12* variants have recently been established as a definitive cause of PCD, and affected individuals typically present with recurrent sinopulmonary infections, chronic cough, and bronchiectasis [2,3]. Together with bone marrow failure, chronic productive cough, recurrent sinopulmonary infections, and the identified *FANCA* and *TTC12* variants, these findings strongly supported a dual diagnosis of FAA accompanied by *TTC12*-related PCD. The patient was evaluated by pediatric hematology, pediatric pulmonology, and clinical genetics teams. He underwent HSCT, receiving a preparative regimen consisting of fludarabine at 120 mg/m² from day -10 to day -6, low-dose cyclophosphamide at 5 mg/kg/day from day -5 to day -2, and a rabbit antithymocyte globulin total dose of 20 mg/kg (5 mg/kg/day) from day -4 to day -1. Fludarabine-based low-intensity conditioning protocols

are now widely recommended for patients with Fanconi anemia due to their reduced toxicity and favorable engraftment outcomes [4,5]. Cyclosporine A and methylprednisolone were given for graft-versus-host disease (GVHD) prophylaxis. The patient was transplanted with bone marrow from his HLA 10/10-matched brother, who was wild-type for both variants. The dose of total nucleated cells was 3.35×10^8 /kg and CD34 was 4.96×10^6 /kg. Antimicrobial prophylaxis was administered with fluconazole, ciprofloxacin, and acyclovir. Neutrophil and platelet engraftment occurred on days +10 and +15, respectively. Post-transplant follow-up revealed no acute or chronic GVHD, severe infections, pulmonary complications (bronchiectasis exacerbation, bronchiolitis obliterans, interstitial pneumonia), or organ dysfunction.

To the best of our knowledge, this patient is the first in the literature with FAA and PCD to be transplanted without complications. The coexistence of FAA and PCD is clinically relevant, particularly in the setting of HSCT. Underlying PCD-associated bronchiectasis and impaired mucociliary clearance may increase the risk of peri-transplant pulmonary infections and long-term respiratory complications. Recognition of this dual diagnosis is therefore important for pre-transplant pulmonary assessment, selection of reduced-intensity conditioning regimens, close respiratory monitoring during transplantation, and structured long-term pulmonary surveillance after HSCT.

Keywords: Fanconi aplastic anemia, Primary ciliary dyskinesia, Hematopoietic stem cell transplantation

Anahtar Sözcükler: Fanconi aplastik anemi, Primer siliyer diskinezi, Hematopoetik kök hücre nakli

Ethics

Informed Consent: The family of the patient signed an informed consent form freely.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.Ö., P.A., B.D., E.Ü.; Concept: M.Ö., E.Ü.; Design: M.Ö., E.Ü.; Data Collection and Processing: P.A., E.Ü.; Analysis or Interpretation: M.Ö., H.B., E.Ü.; Literature Search: M.Ö., B.D., E.Ü.; Writing: M.Ö., E.Ü.

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