Clinical Overview of Fanconi Anemia for ICD-10-CM Committee

ICD-10 Coordination and Maintenance Meeting

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Overview of Fanconi Anemia

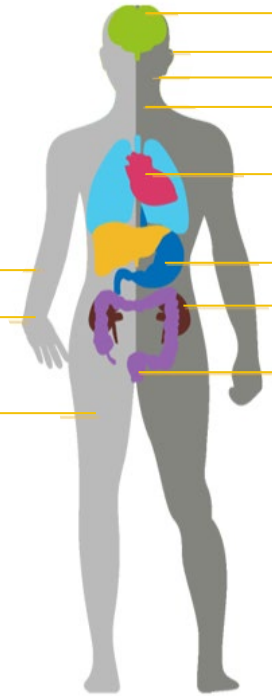
Definition	A **rare, most commonly autosomal recessive, genetic disorder of DNA repair** resulting in chromosomal instability, bone marrow failure, and increased risk of congenital malformations and malignancies
Symptoms	• **Progressive bone marrow failure** (aplastic anemia) • **Congenital malformations**, which may vary in severity across any major organ system • **Increased risk for solid and hematologic malignancies** • **Children with Fanconi anemia have an increased incidence of developmental delays** including learning disabilities, hearing and vision deficits, various endocrinopathies, and growth failure • There are at least **23 different genes which cause Fanconi anemia**[1]; types and severity of symptoms can differ widely in individuals
Outcomes	• **Cytopenias and progressive bone marrow failure occur in early childhood** (mean age of 7 years)[2] • Severe aplastic anemia **may lead to death before 10 years of age**[1] • Over **30% of patients experience hematologic malignancies** (AML or MDS) by age of 40[2]
Prevalence	Though exact prevalence not known, **incidence is estimated at 1:136,000** live births[3]

1. Mehta A, and Ebens C. Fanconi Anemia. GeneReviews. Seattle (WA): University of Washington, Seattle; 2002-2021.
2. Kutler DI, Singh B, Satagopan J, Batish SD, Berwick M, Giampietro PF, Hanenberg H, Auerbach AD. A 20-year perspective on the International Fanconi Anemia Registry (IFAR). Blood. 2003 Feb 15;101(4):1249-56.
3. Che R, Zhang J, Nepal M, Han B, Fei P. Multifaceted Fanconi Anemia Signaling. Trends Genet. 2018 Mar; 34(3)171-183.

Multi-systemic Presentation in Patients with Fanconi Anemia

Overview of Clinical Presentation

How does FA affect the body?



Psychosocial effects
Development delays
Hearing loss
Oral cancer
Head and neck cancer

Heart malformations

Digestive difficulties

Kidney & urinary tract malformations

Reproductive issues
Vulvar cancer
Anal cancer

Shorter or missing radius

Hand & thumb abnormalities

Whole body:
Abnormal blood counts
Bone marrow failure
Leukemia
Dermatologic issues
Hormone deficiency
Short stature

People with FA may experience any combination of these symptoms, ranging from one, to many.

Source: Fanconi Anemia Research Fund
www.fanconi.org/images/uploads/other/All_About_FA_2021.pdf

Diagnosis, Management, and Treatment

Diagnosis

- Definitive test for Fanconi anemia is a chromosome breakage test
- VACTERL* syndrome malformations; marrow failure, myelodysplasia, acute myeloid leukemia, or squamous cell carcinoma in a young adult are common indicators of Fanconi anemia
- Diagnosis is missed or delayed in >70% of patients[1], which limits opportunities for routine surveillance and monitoring

Treatment

- Allogeneic hematopoietic stem cell transplant (HSCT) is the only curative treatment option for hematologic manifestations of Fanconi anemia.
  - However, incidence of solid tumors and time to onset, most often squamous cell carcinoma of the head and neck, are significantly increased in patients who have undergone HSCT
  - Due to this increased risk, HSCT is reserved for patients with severe bone marrow failure, myelodysplastic syndrome, and leukemia
- Surgery may be the best course of treatment for patients who develop cancers due to underlying sensitivity to chemotherapy and radiation, as well as to address congenital malformations

Management

- Patients are managed by multidisciplinary team of specialists, most commonly hematologists, endocrinologists, dermatologists, and head and neck and gynecologic (females) surgeons, as well as potentially other surgical subspecialties
- Management of Fanconi anemia patients includes minimizing exposure to DNA damaging events:
  - Fanconi anemia patients undergoing cancer treatment must receive modified chemotherapy and/or radiation doses
  - Fanconi anemia patients must avoid ~~as~~ sun exposure, alcohol, and radiation (e.g., CT scans or x-rays)
  - Without expedient diagnosis, patients may have significant negative health consequences due to lack of surveillance for bone marrow failure, leukemia, and cancer, as well as lack of or insufficient coordination of care
  - The absence of a diagnostic code increases the potential for patients' exposure to DNA-damaging events by providers who may not be aware of the specific management requirements required by Fanconi anemia patients

*Vertebral anomalies, Anal atresia, Cardiac abnormalities, Tracheo-esophageal fistula, Renal anomalies, and radial Limb

1. Wu ZH. The concept and practice of Fanconi Anemia: from the clinical bedside to the laboratory bench. Transl Pediatr. 2013 Jul;2(3):112-9.

Fanconi Anemia Summary

- Fanconi anemia is a rare, genetic disorder of DNA repair It is characterized by bone marrow failure, predisposition to malignancies, and congenital malformations
- Late diagnosis frequently leads to exacerbated disease complications and postponed initiation of monitoring and insufficient coordination of care
- Patient management must ensure minimization of exposure to DNA damaging agents as well as frequent monitoring for disease complications, requiring all treating professionals to be aware of a patient's Fanconi anemia diagnosis
- The creation of an ICD-10 code will facilitate use of appropriate monitoring and treatments and limit use of inappropriate, DNA damaging treatments by physicians and providers by ensuring HCPs are aware of the patient's diagnosis

Thank You

Questions?