Chapter 14

The Adult Fanconi Anemia Patient

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Introduction

Adult FA patients (≥18 years of age) are an increasing proportion of the general FA population. This group consists of individuals diagnosed and treated in childhood and those newly diagnosed as adults. The former group is growing as a result of increased recognition and testing, combined with better transplant results and improved supportive care options. The latter is growing as a result of wider testing of family members and increased testing and diagnosis of adult patients who present with FA medical issues, such as head and neck cancer at younger than expected ages. These two groups have both common and divergent needs and issues. Some adult patients are transplant survivors while others are not transplant candidates or have refused transplant, further highlighting the diverse profile of the adult FA population.

Major health care issues in the adult FA population have been described in general database reports by the International Fanconi Anemia Registry (IFAR) and a North American Survey (NAS) based at NIH.[1-3] Some of these issues are already recognized as unique to the adult FA population. However, to date, the adult population has not been studied as a group in prospective studies.

In this chapter, we will review the specialized needs of the adult FA patient, emphasizing the required multidisciplinary nature of the care team. The current paucity

of data does not permit a comprehensive approach to specific medical concerns, as many issues are just beginning to be recognized and evaluated. However, we have commented where there is sufficient information and have referenced other chapters where appropriate.

General Considerations

Whether addressing patients diagnosed in childhood or newly diagnosed, the initiation of an appropriate management plan for an adult with FA begins with a complete survey of medical issues in a patient age-appropriate manner. Issues will differ by degree of prior evaluation and treatment, current symptom complex, and the evolving clinical database pertinent to this patient group. The provider will need to consider age-specific issues (e.g., hypertension, lipid profile, fertility, sexual functioning) as well as FA-specific issues (e.g., increased cancer risk) and treatment-specific issues (e.g., cataract risk after transplant, transfusional iron overload) and the potential interactions of these three fields. For the adult patient, management of expectations, family dynamics and external drivers, such as workplace and social environment, are likely to be critical components of care. Experience in other disorders highlights that the need for a clear definition of the relative roles and responsibilities of the care team and the patient is particularly relevant for individuals diagnosed in childhood and historically managed in the context of (surrogate) parental decision-making.[4] In contrast, the newly diagnosed adult patient has a far different need for education and for assistance in addressing alterations in workplace, community, and family relationships.

The medical consequences of FA itself in aging patients are poorly described, as are the consequences of the

treatments administered to affected children surviving to adulthood. This knowledge gap affects not only the development of the best medical plan, but also confounds a clear delineation of expectations at any point in the patient's adult experience. Further, the current data shed little light on the efficacy or tolerability of general medical treatments commonly used in adult patients when used in adults with FA. Such information will be a critical part of managing the issues listed below, as well as additional needs and problems to be defined.

Hematologic Issues in the Adult FA Patient

The currently recognized, non-transplanted adult FA population is small. Although a few of these patients have not developed bone marrow failure or hematologic malignancies, and some may not do so in their lifetimes, all require scheduled hematologic evaluations (see Chapter 3). Those adult non-transplanted FA patients with bone marrow failure may require treatment and/or transfusions and will require frequent evaluation for the development of hematologic malignancies. They may also be at risk for iron overload and need chelation or may be chronically chelated and require management of chelation side-effects (see Chapter 3). Importantly, the improving results of transplantation, particularly from unrelated donors, suggest that transplantation will remain an option for many of these patients. The dialogue regarding a possible decision to proceed to transplant should be informed by the most current transplant results in adult patients and requires continuing education and counseling of affected individuals.

Even patients who have undergone transplantation may have hematologic issues. There is a small chance of

hematologic relapse in these patients, for which they require continued hematologic evaluation. Long-term use of medications and chronic graft-versus-host disease may affect hematopoietic functioning. Ongoing evaluation of chimerism may be indicated.

Solid Tumors in the Adult FA Patient

This issue is discussed in depth in Chapters 6 and 13 and is perhaps the most significant health issue recognized to date facing the adult FA patient. In particular, squamous cell cancers of the head and neck, and cervical and vulvar cancers in women, occur at remarkably high rates and at younger than expected ages. An estimated 1/3 of FA patients will develop a solid tumor by the age of 48, most in the 2nd and 3rd decades of life.[3] These cancers may occur even earlier in transplanted patients.[5] Patients must be continually re-educated regarding this complication and be screened by an educated specialist. FA specialists should be consulted when these tumors are diagnosed, because treatment of these cancers may require different treatment modalities than used for the same cancers in non-FA patients. Behaviors increasing risk for these malignancies, such as smoking and alcohol consumption, should be discussed as part of a pre-emptive strategy.

The role of human papillomavirus (HPV) in the genesis of these cancers in FA patients remains a topic of debate, but one that is likely to be settled in the next few years. Consequently, patients should be appropriately counseled in regard to the potential of HPV vaccination to prevent HPV infections (and subsequent cancers) in the cervix and oropharynx. The benefit seems likely to be as great or greater than that of the general population, although the data regarding the ultimate cancer-preventing efficacy of these vaccines

in any population remain to be determined. In addition, the incidence of other tumors, including gastrointestinal and breast cancers in particular, may be excessive. The evolving data will need to be carefully evaluated to develop appropriate monitoring (and treatment) strategies that respect the desire to minimize radiation exposure and treatment-related toxicity.

Gynecologic and Fertility Issues in the Adult FA Patient

Discussions of expectations regarding fertility and life-expectancy are obviously quite different with an adult patient than with a child and his/her parents. Adult FA women experience early menopause, need high-risk management of pregnancies, and have an increased risk of gynecologic malignancies (see Chapter 6). Adult FA men are generally azoospermic and infertile. Advances in assisted reproduction techniques have led to new possibilities for the prevention and treatment of infertility. Early referral to a fertility clinic may be warranted. These issues may be particularly challenging to address with newly diagnosed patients.

Diabetes and Vascular Health

While the data on glucose intolerance are becoming better described in children with FA (see Chapter 7), the natural history in FA adults is unknown. In addition, the effects of oral hypoglycemics developed for the general population will need to be evaluated in this patient subgroup.

The interaction of FA with vascular disease of aging is unknown. Long-term follow up studies of children surviving transplant, as well as other cancer treatments, suggest that vascular and cardiac disease incidence will

be increased. However, the best practice for following and managing patients is unknown and will need to be established by collaboration between various expert providers. Further challenges in these areas will be provided by integrating the side-effects of prior and ongoing therapies with management of these, and other, results of normal aging.

Transition of Care

Transition of care from pediatric to adult medicine is an important issue in young adults with complex and chronic illnesses.[4,6,7] Although the authors are not aware of specific transition programs for young adults with FA, evidence supports the benefits of an anticipated and coordinated transition process.[4,7,8] Effective transition programs have been developed in other chronic illnesses, such as cystic fibrosis, diabetes, juvenile idiopathic arthritis, and sickle cell anemia. European countries with comprehensive state-supported health care systems have often taken the lead in the development of these transition systems.

Transition of health care is important for two main reasons:

1. In most centers, pediatric services define their target population by age, and adults may not be treated by pediatric subspecialists or in pediatric in-patient facilities. This is obviously dependent on the locality and varies widely.
2. Young adult patients must develop independence and undertake personal responsibility for their health care.

Timing of transition is important and must be seen as a process, not an abrupt transfer of services. Data show

that the most successful transitions are initiated at a very early stage with prospective education of the family and patient regarding future transition.[4,8] As this process proceeds and adolescents take on more health care responsibilities, they should be involved in education and decision-making. The timing should be individualized and not dependent on age. In contrast, timing may be very situation-dependent, as it is likely to be inappropriate to transition a patient with quickly progressing disease or at the "end of life."

As more FA patients reach adulthood, the management and development of transition of health care services are becoming increasingly important and must be addressed on a national level. Focus groups and surveys have identified barriers to transition,[4,7,8-11] including:

- Reluctance of patients and their families to leave trusted health care providers and comfortable clinical settings.
- Differences in approaches to the chronically ill by pediatric and adult providers; i.e., family medicine with prospective multidisciplinary support versus expectation of adult independence and self-reliance with more focused requested support.
- Concerns about the experience, knowledge base and quality of care that will be offered by specialists in adult medicine in regard to childhood-onset diseases.
- Physician reluctance to transition.
- Lack of continuing health care coverage for the young adult.
- Lack of adequate education and preparation of patients and families.

The key element to successful transition is continuous preparation of the patient and family and the identification of a willing and appropriate specialist in adult medicine who can be the primary coordinator of health care issues. The new and prior team should work to define necessary subspecialty providers who either have experience in FA or are willing to be educated as to the needs of this patient population. Because of the rarity of FA, the above goals are often not realistic. In this case, it is essential that an FA specialist remain involved in patient care decisions and be available for consultation, especially regarding the screening and treatment of secondary cancers or other newly recognized issues in adult FA patients. FA patients who have been transplanted may have the option at the larger centers to be followed in long-term survivor clinics where many of their health care needs can be coordinated.

Psychosocial Issues in the Adult FA Patient

The primary psychosocial components involved in growth and development from childhood through adolescence into adulthood are significantly complicated by chronic disease. As in all childhood diseases, surrogate decision-making imposes many demands on parents and guardians. There is a potential risk of parental over-protectiveness in the setting of requisite attention to safety, and the age-appropriate pursuit of adolescent independence may be particularly difficult for parents. The inability to participate fully in childhood activities (i.e., school, sports, and leisure) may isolate FA children and delay development of peer relationships. Recent follow-up of adult survivors of childhood acute lymphoblastic leukemia shows more adverse mental health functional impairment and activity limitations compared with their healthy siblings.[12] In addition, rates

of marriage, college graduation, employment and health insurance coverage were all lower compared to their healthy siblings. We expect that FA adults experience these same issues. Studies to date show that these latter issues of adulthood are also inadequately addressed in many pediatric healthcare settings, thus further exacerbating the stress on patients and families.[4,8]

For these reasons, the adult FA patient diagnosed in childhood may need extensive vocational, educational, and psychosocial support and guidance. High-risk behaviors, such as alcohol and drug use, are common in patients with chronic illness, as in the general population, and have been a major problem in FA adults (Gillio personal communication). Medical compliance may also be an issue, particularly during adolescence and during the transition period. For individuals newly diagnosed in adulthood, the ramifications of established relationships (with spouses, partners, employers, etc.) may be extreme. The magnitude of these psychosocial problems has not been assessed in FA adults and should be assessed in contemporary patient cohorts in the future.

Summary

The growing population of adult FA patients presents particular challenges to the community of FA care providers. The knowledge base is as yet insufficient for understanding best practices, and the provider pool within the community of physicians caring for adult patients is not yet well educated as to either the nature of the disorder or the needs of the patients. This places great responsibility on FA specialists in terms of education of patients and other providers, coordination of transitional care, and addressing the research needed to develop information to assure the best outcomes for patients.

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