Jacobsen Syndrome in a Patient with Combined Immunodeficiency, Thrombocytopenia, and Lymphoma

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To the Editor:

I read the case report entitled 'Immunodeficiency and lymphoma in Jacobsen syndrome' by Nigolian et al [1] with great interest. I have a few questions and concerns about the authors' case presentation and feel that greater detail would be helpful for the readers of your journal.

Immunodeficiency (both humoral and combined) is a very well-known entity in Jacobsen syndrome (JS) that has been described elsewhere [2]. The title of the case report may lead the reader to assume that immunodeficiency is newly defined in this syndrome. The authors first stated that the patient was thought to have transient immunodeficiency and later received intravenous immunoglobulin (IVIG) replacement therapy (0.4 g/kg/mo) for recurrent infections from the age of 8 until the age of 12 [1]. The authors further hypothesized that chemotherapy exacerbated the patient's immunodeficiency. They do not fully address the status of the patient's immunodeficiency. The diagnosis was delayed at least up to 8 years. We do not know what happened to his immunodeficiency between 12 and 46 years of age. It would be interesting to know if the patient is still receiving IVIG replacement therapy.

The patient seems to have combined immunodeficiency and probably requires lifetime IVIG. There are no previous laboratory values for the patient's hematologic and immunologic status (serology and flow cytometry data). The Table shows hematologic and immunologic laboratory values after chemotherapy. However, it would be interesting to see the data from before chemotherapy [1]. Therefore, for the reader, the type of immunodeficiency the patient had and has is slightly unclear.

Although it is very important to report and be aware of the development of lymphoma in JS, the risk of malignancy in children with primary immunodeficiency disease (PID) is reported to be 4%, which is 10 000 times higher than in healthy individuals of a similar age [1,2]. This natural progression in some PID patients was not mentioned in the article [2,3]. I agree that more should be known about this phenomenon and that clinicians' attention should be drawn to the need for careful follow-up in patients with these kinds of PID.

Chemotherapy (R-EPOCH) in an immunodeficient patient is sometimes problematic and difficult to choose [3,4]. For instance, the literature would benefit from knowing whether the authors reduced the dose or added to or changed the standard chemotherapeutic regimen. It would also be interesting to know how long they have been following the patient up since he completed chemotherapy. Have there been any recurrences due to PID?

I wish to emphasize that the differential diagnoses for JS include Turner and Noonan syndromes, as well as acquired thrombocytopenia due to sepsis. In the diagnosis of patients with these syndromes, JS should be kept in mind and immunodeficiency should be sought. Differential diagnoses were not mentioned at all in the article [1].

I am not sure if the typical features of JS (trigonocephaly, platelet disorder, heart abnormalities) are complete or not in this patient. The patient probably had trigonocephaly and platelet disorder, although there is no mention of congenital heart abnormalities [1]. Studies in humans and genetically engineered mice suggest that deletion of the gene *ETS1* (E26 transformation–specific sequence 1) is the cause of congenital heart defects in JS, although the underlying molecular and cellular mechanisms are unknown [5]. Again, readers may wish to know if the patient had a heart abnormality.

I detected a typesetting error: "hypogammaglobulinemia" has been written as 'hypogammaglobinemia' [1]. There is also a mention of transient immunodeficiency in childhood. A better description of this disorder is transient hypogammaglobulinemia of infancy [6]. Transient immunodeficiency of childhood might be due to various diseases, eg, sepsis, rather than transient hypogammaglobulinemia of infancy.

The case report should have emphasized the lateness of the diagnosis of JS, the need for a full differential diagnosis in JS, and the fact that immunodeficiency is part of this syndrome.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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