False Positive Galactomannan Test after Ice-Pop Ingestion

TO THE EDITOR: A 42-year-old woman received an HLA-matched hematopoietic stem-cell transplant from an unrelated donor for a myeloproliferative syndrome. Serum aspergillus antigen (galactomannan) (Bio-Rad Laboratories) was assessed twice weekly from the day of transplantation and remained negative (index, <0.5) until 30 days after transplantation. The index increased to 2.22 and 3.01 on days 32 and 34, respectively. At that time, the patient had severe gastrointestinal graft-versus-host disease (GVHD). She was afebrile with no pulmonary or sinus symptoms. Computed tomographic (CT) scans of the lung, brain, and sinus were normal, and a CT scan of the abdomen showed no evidence of invasive aspergillosis. Cultures of sputum samples were negative, as was polymerase-chain-reaction (PCR) assay of the blood for aspergillus.

Voriconazole was initiated on day 35, since no known cause of false positivity for galactomannan was found among concomitant intravenous treatments.[1] However, the patient, who was otherwise fasting, had begun consuming three to four flavored ice pops (i.e., a freezer pop with no stick) per day, starting on day 29 after transplantation. Four flavored ice pops from the same batch were tested for galactomannan; all were positive at several dilutions (index at dilution of 1:4, >5). The patient discontinued the flavored ice pops on day 37, and galactomannan levels returned to negative within 7 days (Fig. 1A). Voriconazole therapy was discontinued on day 53. The patient died from GVHD and cytomegalovirus infection on day 141, with no evidence of aspergillosis.

A total of 37 flavored ice pops of three marketed brands were tested for galactomannan, cultured on Sabouraud's dextrose agar and chloramphenicol, and examined for fungal DNA with the use of a multiplex PCR assay (PLEX-ID Broad Fungal assay, Abbott). Of the 37 cultures, 3 contained penicillium, ranging from one to three colonies. Since all PCR assays were negative, a contamination by penicillium of the wrapping was thought to be likely. High levels of galactomannan were observed in all samples, regardless of brand or flavor (Fig. 1B). A probable prozone effect was observed with all samples (i.e., samples had a negative index when tested in the pure form, but the index changed to positive on serial dilutions).

The source of galactomannan in the flavored ice pops was undetermined because we could not find complete information on the produc-

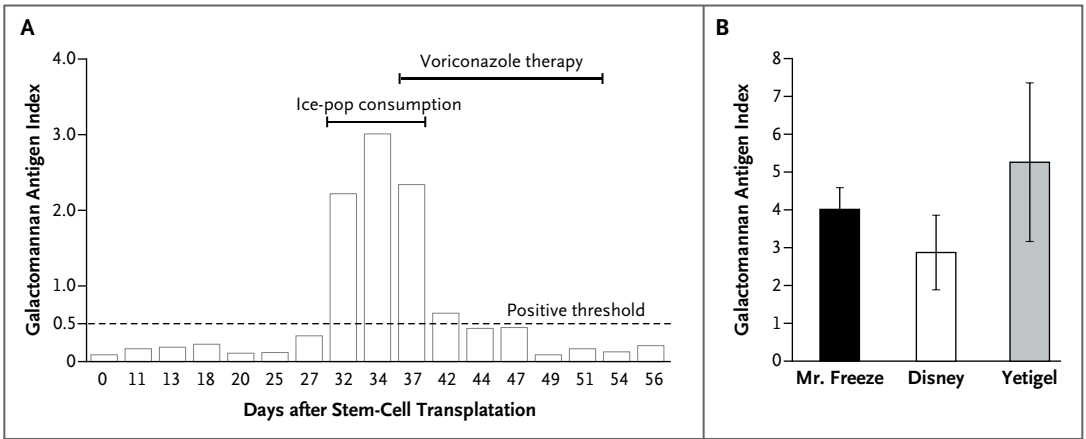

Figure 1. Galactomannan Indexes in the Patient and in Three Brands of Ice Pops.

Panel A shows the patient's galactomannan antigenemia after stem-cell transplantation, with transient false positivity related to the consumption of flavored ice pops. Panel B shows the mean values of galactomannan indexes (Platelia, Bio-Rad Laboratories) in flavored ice pops manufactured under three brand names: Mr. Freeze (Calypso; 15 ice pops sampled), Disney (R&R Ice Cream; 8), and Yetigel (Yetigel International; 14). Samples were tested at a dilution of 1:8. I bars indicate the standard deviation.

tion process. Food additives containing galactomannan can be suspected[2,3] and should be investigated. One possible source is sodium gluconate, which is currently used in Europe and the United States as a thickener and stabilizer for water-based frozen desserts[4] and is known to cause false positive tests for galactomannan.[5] In our patient, a mucosal translocation of galactomannan after consumption of the flavored ice pops is a plausible explanation. Physicians should be aware of this unusual cause of interaction with the galactomannan test, which can result in unnecessary investigations and treatments.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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CORRECTION

Genomic and Epigenomic Landscapes of Adult De Novo Acute Myeloid Leukemia (May 30, 2013;368:2059-74). The source footnote (page 2059) and the Appendix (page 2073) should have begun, "The authors (members of the Cancer Genome Atlas Research Network) . . . ," rather than "The members of the Cancer Genome Atlas Research Network . . . ." The article is correct at NEJM.org.

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