Vinorelbine-Induced Pancreatitis: A Case Report

Vinorelbine is an active agent for the treatment of metastatic breast cancer and non-small-cell lung cancer (1,2). Its toxic effects are well described, but pancreatitis has not been reported. We now report a case in which vinorelbine appears to have caused acute pancreatitis.

A 40-year-old woman was originally diagnosed with advanced breast cancer in 1993. When she developed progressive chest wall and bone metastases in 1995 she was treated with daunorubicin. In January 1996, she developed cardiac tamponade secondary to metastatic tumor and was treated with a pericardial window followed by radiotherapy and subsequently paclitaxel [Taxol]. In January 1997, she began treatment with vinorelbine. Several hours after the first treatment she developed nausea and vomiting. After 4 days these symptoms resolved.

The second course of vinorelbine was given 3 weeks later, and again she developed nausea and severe vomiting. She was hospitalized 3 days after treatment with persistent nausea, abdominal pain, dehydration, and diffuse abdominal tenderness. Plain radiographs were negative. Laboratory studies on admission revealed the following (normal values in parentheses): calcium level, 8.5 mg/dL (8.8–10.8); amylase level, 105 IU/L (30–110); lipase level, 295 IU/L (30–190); and alkaline phosphatase level, 174 IU/L (34–124). Bilirubin and transaminase levels were normal.

She was treated with intravenous fluids, diphenhydramine, and bowel rest. The lipase level increased to 469 IU/L on the second hospital day (see Table 1 for all values). Ultrasound and computed tomography scan of the abdomen were normal. The patient’s symptoms gradually improved with conservative therapy, and on the 11th hospital day she was discharged. No further vinorelbine was administered.

This patient’s clinical and laboratory course are consistent with a drug-induced acute pancreatitis. She gave no history of alcohol use, and there was no evidence of calculus disease. The only other medication that she had recently used was an oxycodone/acetaminophen combination, which had been used intermittently for several years.

A literature review revealed no other cases of vinorelbine-induced pancreatitis, although nausea and vomiting are commonly seen. It is possible that if amylase and lipase levels were obtained more often, that additional cases might be diagnosed. Many other chemotherapy agents have been occasionally associated with pancreatitis, including paclitaxel, ifosfamide, flouxuridine, cytarabine, and asparaginase and the combination of cisplatin, vinblastine, and bleomycin (3–8). When patients experience prolonged nausea, vomiting, or abdominal pain, amylase and lipase levels should be determined.

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References


Notes

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Table 1. Serial amylase and lipase determinations

<table>
<thead>
<tr>
<th>Hospital day</th>
<th>Amylase (IU/L)</th>
<th>Lipase (IU/L)</th>
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<tbody>
<tr>
<td>1</td>
<td>105</td>
<td>295</td>
</tr>
<tr>
<td>2</td>
<td>109</td>
<td>469</td>
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<td>4</td>
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<td>6</td>
<td>92</td>
<td>331</td>
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<tr>
<td>8</td>
<td>89</td>
<td>238</td>
</tr>
<tr>
<td>11</td>
<td>–</td>
<td>320</td>
</tr>
</tbody>
</table>

*Reference values: amylase, 30–110 IU/L; lipase, 30–190 IU/L.
cient number of patients to answer the question of the use of tamoxifen therapy in this group of patients. The survival advantage is approximately 4% at 10 years, but less than 50% of the patients are at risk at 10 years at the time of this article. It appears that at 8 years there is no survival advantage. Thus, it is conceivable that with further follow-up the survival advantage that is seen at 10 years may change. Furthermore, the subanalysis of women who are 50 years of age or older, and who represent the majority of the patients in the study, demonstrates that there is no survival advantage over the 10-year follow-up [Fig. 3 survival curve P = .13 (1)]. Are we to conclude that the use of tamoxifen in women greater than or equal to 50 years of age with node-negative estrogen receptor-positive operable breast cancer is not useful in prolonging survival or is it necessary that further follow-up be obtained to see the survival advantage? Although tamoxifen is a relatively benign form of treatment, there are side effects associated with it, including hot flashes and an increased incidence of thrombosis. Furthermore, many gynecologists, because of the increased risk of endometrial cancer, are performing routine endometrial biopsies that are quite painful for the patient. Thus, it is critical to know whether the use of this drug is truly improving the survival of such patients as reported in this study.

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Response

We appreciate the interest of Drs. Panasci and Melnychuk in our article and understand their concerns with regard to the necessity to determine a survival advantage from tamoxifen. The overall survival curve shown in our article indicates that survival distributions in the two groups were within 1% at 8 years. However, the difference in survival that begins to emerge at 4 years results in a significant survival benefit cumulatively through 10 years.

Our primary purpose in showing treatment comparisons by age was to illustrate the consistency in response among younger and older patients, since, for some time, there has been concern about the efficacy of tamoxifen in premenopausal women. Our statement that the interaction between treatment response and age group was nonsignificant (1) indicates the absence of statistical evidence of a difference in reduction in mortality by age group for patients receiving tamoxifen. Although the B-14 study included a very large number of patients, the ability to detect statistically significant differences in survival rates among groups is determined by the number of deaths observed. We would expect that, examining subgroups of patients who have insufficient events to provide adequate statistical power for reliable comparisons, nonsignificant results may be obtained.

Survival results from our article are generally consistent with the Early Breast Cancer Trialsists’ Collaborative Group overview results (2). Their 1992 report indicated a roughly 17% decrease in mortality rates for women with node-negative breast cancer. A survival benefit was noted for patients receiving tamoxifen, irrespective of age group or nodal status. Recent large tamoxifen studies of moderate duration compared with shorter duration are also consistent with an advantage for 5 years of tamoxifen in older women (3,4).

In summary and in response to the question raised by Drs. Panasci and Melnychuk, our study results suggest a modest survival advantage and a large reduction in total events for both younger and older patients who receive tamoxifen. This finding is consistent with the world literature on tamoxifen efficacy.

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References


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Re: Probability of Carrying a Mutation of Breast–Ovarian Cancer Gene BRCA1 Based on Family History

Computing the posterior probability that a person carries a cancer susceptibility gene based on family history is useful for genetic counseling, selection for genetic screening, and individualized predictions of future cancer occurrence, so a generic computational approach would be useful. Berry et al. (1) presented Bayesian predictions that a person carries the BRCA1 breast cancer gene, posterior to consideration of family history up to only second-degree relatives (2). When age at cancer diagnosis can merely be restricted to an in-