Severe Veno-Occlusive Disease in an Overweight Infant With a Renal Tumor

To the Editor: An overweight (16 kg) 19-month-old male was recently diagnosed with a left-sided renal tumor and subsequently with a 2-day history of hypoactivity and decreased oral intake. He began a chemotherapeutic regimen of actinomycin D and vincristine alternating with vincristine at weekly intervals for four cycles based on the SIOP 93–01 protocol. His fourth week of chemotherapy was completed 2 days prior to admission.

He was ill-appearing, lethargic, and had hepatomegaly. Laboratory investigations revealed hypoglycemia (serum glucose of 30 mg/dl), elevated lactic acid level (5.4 mmol/L), high prothrombin time (PT) 25 sec (<11.4) and partial thromboplastin time (PTT) 39 sec (36 sec) and elevated D-dimer plasma level. Total bilirubin was 2.8 mg/dl (<1) and direct bilirubin was 1.7 mg/dl; both ALT and AST were normal. He was admitted to the intensive care unit and started on broad-spectrum antibiotics.

Twenty-four hours after admission, the patient deteriorated clinically and repeat investigations revealed bilirubin of 5.9 mg/dl, direct bilirubin 2.9 mg/dl, AST 3369 IU/L, ALT 1727 IU/L, hemoglobin 5.3 g/dl and platelet count 22,000/mm³. An abdominal ultrasound (US) showed enlargement of the liver (9 cm in length) and mild ascites. Hepatic veno-occlusive disease (VOD) was suspected given the clinical and laboratory features of acute liver failure. Despite full supportive measures he continued to clinically deteriorate and ultimately progressed into multi-organ failure, which led to his death in <72 hr from presentation.

Among the most serious side effects of Wilms tumor chemotherapy regimens is hepatic VOD, which is reported in ~5% of children treated for this tumor [1]. Our patient developed VOD only 4 weeks after administration of chemotherapy and before undergoing a nephrectomy. The criteria for diagnosing VOD include: (1) jaundice (bilirubin >2.5 mg/dl), (2) development of hepatomegaly (>3 cm in mid clavicular line) or right upper quadrant pain, and (3) ascites or unexplained gain in weight of more than 2% [2]. Early development of severe hepatic toxicity is a known risk of preoperative chemotherapy [3,4] and should be considered when treatment is initiated for suspected Wilms tumor. As the family of our patient refused autopsy, confirmation of the actual pathology was not possible.

While small children with body weight <12 kg are at greatest risk for developing VOD [3], our patient was obese, suggesting the possible role obesity plays in the development of VOD. Although various pharmacodynamic and pharmacokinetic properties of drugs can be affected by body weight, no clearly defined recommendations exist on appropriate dosing of chemotherapy in obese children. Table I shows the chemotherapeutic drug dosing used to treat our patient with average weight for age used for calculation. Pharmacological studies examining the effects obesity has on drug properties are very limited. Furthermore, obesity with the accompanying increase in volume of distribution may affect drug clearance in a manner that varies from drug to drug [5,6]. Consequently, obese children may be at greater risk of developing toxicities associated with chemotherapy [5,6].

<table>
<thead>
<tr>
<th>Body parameters</th>
<th>Vincristine (1.5 mg/m²)</th>
<th>Actinomycin D (0.045 mg/kg)</th>
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</thead>
<tbody>
<tr>
<td>Weight 16 kg, height 85 cm, body surface area 0.61 m²</td>
<td>0.92 mg</td>
<td>0.72 mg</td>
</tr>
<tr>
<td>If patient weight was at 50% for age (11.9 kg, surface area 0.53 m²)</td>
<td>0.53 mg</td>
<td>0.35 mg</td>
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</tbody>
</table>

Further 33% reduction for body weight <12 kg.

REFERENCES


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