Case Report

Wilms tumor associated with consumption coagulopathy: A case report and review of the Literature

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Abstract

We present a 16-month old boy who presented with a left nephroblastoma and developed haematochezia and frank total haematuria while awaiting surgery. Clotting profile was consistent with consumption coagulopathy and failed to normalize with repeated blood transfusion. However, coagulation abnormalities normalized after a circle of cytotoxic chemotherapy. Despite the rarity of this haematological abnormality among patients with Wilms tumor, routine initial laboratory evaluation of a child with Wilms tumor should include clotting profile and pre-operative cytotoxic chemotherapy commenced in view of the high surgical risk of a patient with abnormal clotting profile.

Keywords: Neoplasm, Coagulation defect, Nephroblastoma, Child, Zaria.

Introduction

The association of coagulation defect with various malignancies is well established, with thrombosis and hypercoagulability reported in as many as 60% of patients with malignancies[1]. Abnormalities of haemostasis are present with solid malignancies like small-cell carcinoma of the lungs, neuroblastoma, gynaecological malignan-cies1 etc. Among Paediatric solid tumors, associated consumption coagulopathy has been reported with neuroblastoma, rhabdomyosarcoma and histiocytosis X[2,3]. The association of coagulation defects with Wilms tumor is a rare clinical entity. We report a case of Wilms tumor with a coagulation defect that responded to cytotoxic chemotherapy.

Case Report

A 16-month old boy presented with a 1-month history of slowly progressive painless abdominal swelling which was not associated with fever or any other gastrointestinal symptoms. There has been no history of weight loss or urinary symptoms. Examination revealed a well looking child, well preserved with an obvious left loin mass extending to the left iliac fossa. The mass was firm, non-tender and bimanually palpable measuring 10 cm by 8 cm. Laboratory findings included a haemoglobin concentration of 11.0 gm/dl, white blood cell count of 3.6 x 109/L (Neutrophils 47%, Lymphocytes 53%) and Platelet count of 124.0 x 109/L. The Blood Urea Nitrogen was Urea 4.1 mmol/L; Na+ 146 mmol/L, K+ 5.3 mmol/L, Cl+ 106 mmol/L and HCO3- of 25 mmol/L. Serum creatinine, liver enzymes and serum bilirubin were all within normal ranges. Abdominal ultrasound showed normal liver, gall bladder, spleen, para aortic areas, right kidney and the urinary bladder. The left kidney was normal in position and outline but grossly enlarged, measuring 13.5cm in bipolar length (right kidney 7.3cm) with loss of the corticomedullary differentiation. Intravenous urography showed a normal right kidney while the left kidney was faintly outlined, showing displaced and amputated calyces. A diagnosis of left sided nephroblastoma was made and a left nephrectomy was planned. While awaiting surgery, patient started passing blood in

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Table 1:
Clinical summary of cases of Wilms tumor associated with consumption coagulopathy

Source	Age & Sex of Patient	Mode of Presentation	Histology of tumor
Wang et al 1972	5 years (F)	Periumbilical abdominal pain, vomited coffee ground gastric content	Well differentiated right kidney
Peterson et al 1982	3 years (F)	Life long history of easy bruisability	Anaplastic with sarcomatous element, left kidney
Ogawa et al 1983	4 years (M)	Gross haematuria	Poorly differentiated sarcomatous, left kidney.
Procianoy et al 1986	16 hrs (M)	Jaundice, abdominal mass Purpura on trunk	Left kidney.
Singh et al 2003	6 mths (F)	Left lower abdominal mass Purpuric patches	Histology not stated left kidney
Present Case	16 mths (M)	Painless abdominal mass frank haematuria while on admission	Well differentiated, left kidney.

stool and 48 hours later, it became associated with frank total haematuria, occasionally with passage of clots that led to urinary retention necessitating passage of urinary catheter. Clotting profile showed delayed Prothrombin time (PTT) of 37 seconds (control 14 seconds) and Kaolin Cephalin Clotting Time (KCCT) of 65 seconds (control 32 seconds), platelet count was 101 X 109/L and haemoglobin concentration was 8.0 gm/dl. Other clotting profiles such as Fibrin- degradation product, elevated D-dimmer could not be assayed due to lack of laboratory facilities. Clotting profile remained delayed after series of blood transfusion with fresh whole blood. In view of the high surgical risk therefore, a pre- operative chemotherapy with Vincristine and Actinomycin D was given. After a complete cycle of chemotherapy, the clotting profile normalized, the PTT Time being 15 seconds (control 15 seconds) and the KCCT 32 seconds (control 32 seconds). At nephrectomy, an enlarged left kidney was found with tumor not extending beyond the capsule. Cut section of the specimen showed gray, dark and cystic areas. Histology showed epithelial, blastemic and stromal components forming tubules and glomeruli in a fibromyxoid stroma with foci of neural tissue, smooth muscle cells, lobules of adipocytes and cysts. A diagnosis of well-differentiated nephroblastoma was made. Patient received 4 other cycles of cytotoxic chemotherapy. He has since been discharged and is well on follow-up.

Discussion

In 1972, Wang et al [4] reported a case of Wilms tumor associated with fatal venous thrombosis and consumption coagulopathy in a 5-year-old white girl. The authors reviewed the literature and found no report of Wilms tumor with consumption coagulopathy. Two years later, Komp[5] evaluated 40 children with diverse disseminated solid tumors, including 5 with nephroblastoma, and found none with consumption coagulopathy. Also in 1983, Yakubu et al[6] reviewed 44 cases of Wilms tumor in Northern Nigeria over a 9 years period, with 29 of them (65.9%) of stage III and beyond, and found none with consumption coagulopathy. Since the report of Wang et al[4], 4 other cases of Wilms tumor associated with consumption coagulopathy have been reported in the English literature[7-10]. A summary of the cases of Wilms tumor with coagulopathy is shown in table 1.The age distribution of these children (average of 2.3 years) is similar to the general population of children with Wilms tumor where the peak incidence is between the second and third year of life with 70% of children less than 5 years at the time of diagnosis[11-13]

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The male to female ratio of children with Wilms tumor is 1.2:1[12-13] although others have reported equal sex distribution[14] or a slight female preponderance[15]. Although the number of children with coagulopathy is small, the male to female ratio is 1:1 may suggest that sex of the child is not likely to be a contributory factor. The left kidney is involved in 66.7% of children with Wilms tumor associated with consumption coagulopathy, which is slightly higher than the 55% reported for the general population of children with Wilms tumor[13]. The pathogenesis of coagulopathies in malignancy is not well understood. A hypercoagulable state can occur in patients with malignancy if thromboplastic material liberated from the tumor itself or from necrotic tissue within it triggers clotting process[15] or malignant cells enter the circulation[16]. It is therefore expected that blood coagulation abnormalities may be present in patients with disseminated Wilms tumor. It is only in 1 out of the 5 cases (20%) of Wilms tumor associated with consumption coagulopathy (Wang et al[4]) that the tumor was found to extend beyond the capsule into the renal vein. In our patient, the tumor has not extended beyond the capsule. In the series by Yakubu et al[6] extensive abdominal masses, which at laparatomy showed metastases to several abdominal organs, were the main findings, of which 65.9% were of stage III and beyond. Coagulation abnormality was not reported in these children with disseminated tumor. While dissemination of tumor does not appear to be a significant factor in the aetiopathogenesis of consumption coagulopathy in children with Wilms tumor, this need to be further evaluated. The histologic types of this population of Wilms tumor as shown in table 1 included both the poorly and well differentiated tumor, similar to the general population of children with Wilms tumor, which suggests that tumor histology might not be a factor in the aetiopathogenesis of the consumption coagulopathy. While the precise pathogenesis of this blood coagulation abnormality in Wilms tumor is not clear, the coagulation abnormalities is usually corrected with cytotoxic chemotherapy[10] or surgical removal of the tumor[7,9]. The clotting profile of our patient normalized after a single cycle of cytotoxic chemotherapy.

The out come of disseminated intravascular coagulation (DIC) depends mainly on the triggering disease as such, the most important guiding principle for therapy of DIC is to identify the triggering disease and manage it aggressively[17]. The other main therapeutic options in a patient with DIC include blood component therapy, inhibitor therapy and use of antifibrinolytic agents. Because our patient was bleeding, blood component therapy was favored. However, because our blood bank does not have a blood component separator, we were unable to give blood component such as fresh frozen plasma or platelet concentrate. Heparin is an effective anticoagulant but studies have shown benefit[18], no benefit[19] as well as adverse effect[20] when used in patients with DIC. A potential risk with heparin therapy is bleeding. Our patient was bleeding. Other inhibitors of coagulation such as Activated Protein C (APC), Tissue Factor Pathway Inhibitor (TFPI) and Hirudin were not available. Activated protein C can improve DIC more efficiently than Heparin without increasing bleeding[21]. TFPI is a specific inhibitor of tissue factor VIIIa complex and improves outcome more in patients with sepsis[22]. Antifibrinolytic agents such as epsilon-aminocaproic acid and Tranexamic acid are treatment modalities that are of particular importance where primary activation of fibrinolytic systems is involved[23].

The standard treatment of Wilms tumor may consist of surgery followed by chemotherapy or preoperative chemotherapy before surgery, depending upon the condition of the patient and the area of the world the patient is treated. While the National Wilms Tumor Study Group (NWTSG) believes it is vital to identify accurate tumor staging by immediate surgery, the International Society of Paediatric Oncology (SIOP) favors reduction of surgical risk of immediate nephrectomy by

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preoperative chemotherapy[24]. Despite the surgical risk in a child with Wilms tumor with coagulopathy, coagulation studies need not be routinely performed because of the rarity of consumptive coagulopathy but if there is any sign of clinical bleeding or indication of an abnormal laboratory test, coagulation studies should be performed and, if they are abnormal, preoperative chemotherapy considered as the most appropriate treatment since it poses less risk to the patient and coagulation abnormalities usually correct.

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