METASTATIC WILMS TUMOR WITH A SURPRISING RESPONSE TO A DIFFERENT MANAGEMENT – CASE REPORT

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Abstract

Pediatric oncology is an intense field of study in our century, with new developments and changes being made constantly. The management of children with cancers involves, as it does for the adult population, a multidisciplinary team including pediatric surgeons and oncologist, but nevertheless the results are not always satisfying and sometimes difficult to achieve. We report the case of a 6-year-old boy who was admitted to our hospital for acute abdominal pain, in the right upper quadrant. After several paraclinical investigations, it was concluded that the pain was determined by an aggressive form of cancer that had spread to the liver and lungs and invaded the abdominal cavity and pelvis. The biopsy revealed a desmoplastic small-round-cell tumor. He was then referred to an oncologist and a treatment protocol (which included both chemotherapy and surgical management) was initiated. Finally, 6 months after the first hospital admission, at the histopathological analysis, the primary tumor was diagnosed as Wilms tumor.

Keywords: Wilms tumor, biphasic nephroblastoma, desmoplastic tumor

Introduction

Wilms’ tumor (nephroblastoma) is the most common primary malignant solid tumor of the kidney in childhood [1]. It usually presents as a clinically palpable, painless abdominal mass in an otherwise healthy child. Management consists of surgery for removal of the primary tumor with the kidney, accompanied by chemotherapy and radiotherapy in some cases. The management varies with the staging of the tumor and depends on the results of biopsies when needed [2].

Case presentation

We report the case of a 6 years old boy who presented to the emergency department of „Grigore Alexandrescu” hospital for Children for right upper quadrant pain. At the moment of presentation blood tests and abdominal ultrasound scan were done. The blood tests revealed ESR 60mm/h, fibrinogen 430 mg/dl, hemoglobin 9.1g/dl, hematocrit 27.8%, with no other abnormal laboratory results. The abdominal ultrasound scan revealed a giant mass of 13.5/10/13cm which distorted the right kidney structure and compressed the IVC and the liver, presenting multiple hypoechoic areas and positive Doppler signal. Another tumoral
mass of 56/27mm presenting positive Doppler signal was discovered behind the bladder.

The child was admitted on the surgical ward for more examinations. Further assessment of the mass was decided, and the boy underwent a CT scan with contrast of the thorax, abdomen and pelvis. CT scan revealed multiple intra-abdominal heterogeneous masses presenting necrosis, but not calcified areas as follows: one tumoral mass of 98/90/128 mm pertaining to the right kidney and modifying its architecture almost completely, which displaces the right renal vein, the inferior vena cava (IVC) and infiltrates the right hepatic lobe; one tumoral mass in the median retroperitoneum of 42/38/94mm which displaces anteriorly the IVC, the right renal vein and the pancreas; one tumoral mass of 54/37/41mm between the urinary bladder and the rectum, one tumoral mass of 42/20mm located deep into the pelvis, left to the bladder and one homogeneous mass of 28/22mm in the right hepatic lobe. In the thorax the CT scan revealed a tumoral mass of 13/9mm on the base of the right hemithorax presenting the same morphological features as the abdominal masses, one right tracheal adenopathy, multiple pulmonary micro- and macro-nodules, multiple paraaortic adenopathies and free fluid in the right pleural cavity.

A consult with the oncology department was also obtained which stated that the patient should undergo intensive chemotherapy before any kind of surgical resection attempt. The child was therefore trasferred to the oncology ward. Because the results of bone marrow aspiration and biopsy and tumoral marker panel were inconclusive for any specific type of cancer, the chemotherapy protocol could not be initiated and so both the team of surgeons and pediatric oncologists decided that a biopsy of the giant tumor by classical approach was necessary (beta 2 microglobulin – 2.64 mg/l (normal values 1.09-2.53), urinary vanilmandelic acid – 1.2 mg/24h (normal values 0.1-0.18mg/kg/24h), homovanillic acid – 2.2 mg/24h(normal values <8 mg/24h), NSE – 84.64 ng/ml (normal values <17ng/ml), alpha-fetoprotein negative). Intraoperatively, the following details were observed: a giant, friable intra-abdominal mass which presented a very well-developed neovascularization, multiple metastatic masses in the omentum and a massive quantity of viscous dark red fluid in the peritoneal cavity. Bioptic samples were prelevated from all the elements found. It is now important to mention that the child suffered moderate desaturation on the table when the abdominal cavity was first surgically opened, probably because of the pressure differences and the tumoral infiltration of the tracheal wall but was promptly stabilized with the aid of the pediatric anesthesiologist.

After the biopsy, the boy was transferred to the pediatric oncology department where chemotherapy was initiated following the HRNBL1 protocol: vincristine 1.5mg/m² day1, carboplatin 750mg/m² day1, etoposid 175mg/m²/day/4 hours day1 and 2. During the oncological management a series of standard laboratory investigations, abdominal ultrasound and thoracic radiography were performed in order to monitor the patient’s biological tolerance to the treatment and progression of the tumor. A bone scintigraphy was also obtained which revealed no secondary tumors.

The histopathological examination revealed monomorphic small cells presenting amphiphilic cytoplasm and hyperchromatic nuclei. The population of cells exhibited frequent mitosis and apoptosis; cells structured in islets around the blood vessels. Between the islets there was a high desmoplastic stroma presenting fibroblastic and myofibroblastic cells. Immunohistochemistry tests were done, and the following markers were identified: MIC2 – negative; FLY1 – positive; somatostatin – present in a few tumoral cells; NBP – negative; Ki67 present in 45% of the tumoral cells. The diagnosis after the histopathological exam was DESMOPLASTIC SMALL ROUND CELL TUMOR.

Considering the newly obtained histological result a new chemotherapy plan was established, and the patient received P6 protocol consisting of 5 courses of chemo medication. After the first course (vincristine 1.5mg/m²/day1, cyclophosphamide 2100mg/m²/day1 and 2, doxorubicin 25mg/m²/day 1,2,3) the child developed grade IV neutropenia and fever for which he received meropenem, fluconazole and filgrastim. The evolution was good.

After the second chemotherapy course (vincristine, cyclophosphamide and doxorubicin dosage reduced with 25% considering the
neutropenia) the patient developed an upper respiratory tract infection at home and he was readmitted. The pulmonary x-ray revealed the decreasing size of the right lung masses. The third and fourth chemotherapy courses were administered according to the protocol. All the chemotherapy cycles were followed by filgrastim administration.

Between the fourth and the fifth course of chemotherapy the patient underwent a CT scan in order to evaluate the evolution of the masses. The CT scan showed one heterogeneous tumor of 67/65/75mm in the upper 2/3 of the right kidney consisting of multiple necrotic areas and displacing the liver. Another tumor posterior to the left renal vein of 22/7/25mm was discovered. The 7th segment of the liver presented a heterogeneous mass of 17/7mm. Enlarged lombo-aortic lymph nodes of 7/5mm. In the thorax there were discovered one pulmonary nodule of 6/5mm in the right inferior lobe, near the diaphragm, multiple pleural nodular densifications and some enlarged lymph nodes in the Baret lodge. The imagistic aspect was considered clearly superior to the previous examination.

After the fifth chemotherapy course the patient was scheduled for elective surgery: RIGHT NEPHRECTOMY BY CLASSICAL APPROACH with curative aim. Following the lombotomy meticulous exploration of both the peritoneal cavity and the retroperitoneum was performed and a 10 cm renal mass was observed, especially in the upper pole, solid, firm, with irregular outlines, with imprecise delimitation, with numerous fibrotic adhesions, especially to the liver which made the dissection rather difficult. The liver capsule was infiltrated, but the right adrenal gland was normal looking. No other intra-abdominal secondary tumors were identified as well as no pericaval lymphadenopathies. Right nephrectomy was performed with thorough hemostasis control and complete excision of the tumor. The patient spent a few days in the ICU after the operation, but the evolution was good with him being discharged in good state after 7 days.

A complete pathological and immunohistochemistry analysis was performed to the excised tumor and the results were as follows: round-oval cells with diffuse anaplasia clusters and Ki67 positive in 90% of cell nuclei. The final diagnosis was BIPHASIC NEPHROBLASTOMA. Taking into consideration the histopathological diagnosis and the fact that the patient received preoperative chemotherapy, the pTNM grading was ypT1b.

Discussions

Wilms’ tumor (nephroblastoma) is the most common primary malignant solid tumor of the kidney in childhood [1]. Since the first description of Wilms’ tumor by Wilms in the 18th century, the first nephrectomy by Jessop in 1877 [3] and the addition of radiotherapy in 1915, there have been many advances in the treatment of this tumor, especially in the latter part of the 20th century.

But before any kind of treatment is applied one must make a good diagnosis. Although this type of tumor is not known to pose difficulties in diagnosis in some cases the clinical profile of the patient and the investigations can lead one to approach another path.

In the previously detailed case the patient’s first presentation included a palpable intra-abdominal tumor on clinical examination. Both the ultrasound and the CT scan described a massive tumor pertaining to the right kidney and many other smaller tumors in the abdominal cavity and pelvis. This would raise a high suspicion of stage IV right renal nephroblastoma but the negative tumoral marker panel, the histopathology result and the immunohistochemistry analysis concluded that there was actually a desmoplastic tumor. This is a rare type of cancerous tumor, which rarely affects children and with no case described in the literature at such a small age. This mesenchymal tumor is associated with a unique chromosomal translocation t (11:22) (p13;q12) that involves the ESWR1 and WT1 genes [4]. The prognosis is particularly poor; the three-year survival rate being less than 30 % [5], largely due to the presentation of the majority of patients with metastatic disease. In spite of its aggressive nature, this type of cancer is highly responsive to polychemotherapy treatments, but the relapse rate is really high [6]. The specific oncological management of this kind of tumor is
the P6 protocol [7]. In our case the patient received this therapy and responded incredibly well to it, thus allowing surgery with curative intention.

The question we asked ourselves was why did a tumor that was actually a Wilms’ tumor respond so well to a chemotherapy scheme used for a totally different kind of cancer. The only similarity we found was that the tumorigenesis of both cases is linked to the WT1 gene. This gene is usually expressed in the developing genitourinary tract, thus having an important role in renal development and differentiation [1]. Disorders in the expression of this particular gene may influence the responsiveness of tumors to certain chemo drugs, but this needs further studies in order to objectify it.

Conclusions

This is a case report of a 6 years old boy with the initial clinical and imagistic aspect of a very aggressive cancer, which was further preliminary diagnosed with a highly rare presenting tumor in adults and even more rare in children (the round small cell desmoplastic tumor), treated successfully both ontologically and surgically, only to find out in the end that there was the most common primary malignant solid renal tumor in children – the nephroblastoma. In conclusion all is well when it ends well.

References