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Pediatric adrenal neuroblastoma with extensive renal involvement, An unusual presentation and fatal outcome

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Abstract

In this report, we describe a classical case of Poorly differentiated neuroblastoma, nodular type in a seven years old girl presented with a huge abdominal mass. In this report, we tried to differentiate between them depending on the histopathological features and using panel of epithelial and neuroendocrine markers. Adrenal neuroblastoma as a primary site of origin, should be considered in the differential diagnosis of adrenal masses in children and young adult. Neuropil and ganglionic differentiation are helpful features to recognize neuroblastoma and differentiate them from other small blue cell tumors. The fatal outcome of pediatric neuroblastoma depends on the age and stage of the tumour, which have impact on mortality.

Keywords

neuroblastoma; adrenal; pediatric; fatal outcome

Introduction

Neuroblastoma is a malignant tumor arising from the neural crests and it is related mainly to the sympathetic chain ganglia with affection of adrenal gland in 35% of cases and similar percentage for paraspinal ganglia. In all of these cases, the presentation is mainly with abdominal or retroperitoneal masses. However affection of other sites like pelvis, mediastinum and neck is also reported [1]. Neuroblastoma with an unknown primary was reported in 10% of cases [2]. Neuroblastoma is a common round blue cell tumor affecting infants and young children [3]. In this case report we are presenting a case of neuroblastoma affecting a seven years old female child who presented as a mass in abdomen that was not preoperatively diagnosed. The patient underwent nephrectomy operation and died within few days of the diagnosis. In this report, we discussed the different diagnostic challenges and reviewed the different studies considering neuroblastoma in adrenal gland.

Case Report

In this report, we describe a case of a seven years old female complaining of rapidly growing huge abdominal mass. Ultrasound and CT revealed a large left kidney mass involving the suprarenal gland. The patient underwent radical nephrectomy which includes kidney, overlying supra-renal gland and overlying gerota's fascia including accessible lymph nodes and paraortic group. Gross examination revealed partial replacement of Left kidney by large mass measuring 19x12x10 cm. The residual kidney

tissue measured 6x3.5x3.5 cm (Figure). The cut section of the mass was white-yellow in color with areas of hemorrhage and necrosis with central cystic degeneration with evidence of capsular rupture (Figure 1). Seventeen lymph nodes were dissected including paraortic lymph nodes, out of which ten lymph nodes were positive for tumor metastasis. Microscopic examination of adrenal mass revealed a neoplastic growth arranged in a vague lobular and incomplete nodular pattern separated by thin fibrovascular septa. The tumor cells are exhibiting enlarged eccentric nucleus, vesicular chromatin, and single large prominent nucleolus with a rim of eosinophilic to amphophilic cytoplasm. Some of these cells have indistinct cell borders. Large areas of coagulative necrosis, calcification and hemorrhage are present (Figure 2). Lymphovascular invasion and capsular penetration is also seen. One nodule showed ganglioneuroma separated abruptly from the previously described growth (Figure 3). The neoplasm was involving the adrenal gland, left kidney and adherent to the surrounding pelvic and abdominal wall muscles. The neoplastic cells were strongly positive for: Synaptophysin, Chromogranin, NSE (Neuron Specific Enolase) and CD56. S-100 protein is not expressed in the neoplastic cells but it is highlighted in the Schwann cells and satellite cells present in the fibrovascular septa around the tumor nodules. The neoplastic cells are negative for: LCA, Vimentin, RCC, CD10, EMA, Pan-CK, HMW-CK, Actin, WT-1, HMB-45 and CD99 (Figure 4). According to international neuroblastoma staging system, the case was staged as stage IIB. The previous medical, surgical and family history of similar condition is negative. The patient died few days after operation.

Discussion

In this case, we present an example of a pediatric neuroblastoma, but it is reported in several studies and even in older age (22years) than that seen in our case. Such as that reported in T sujip's et al. study [4] where the patient's age was 52 years. Adrenal gland is a common site of neuroblastoma which may also commonly arise in the abdomen or extra- adrenal sites [5]. While according to Kumar et al., 2010 [6], their patient was a fetus 36 week age of gestation who was born by caesarian section and underwent distal nephrectomy for a mass proved to be neuroblastoma. In our case, the main differential diagnostic categories were Nephroblastoma (Wilm's Tumor), Rhabdomyosarcoma, Malignant lymphoma, PNET, (Table). Nephroblastoma was suspected because of young female gender, large lobulating necrotic and hemorrhagic mass, small to medium-sized neoplastic cells. However, it is excluded by absence of triphasic pattern, and negativity for WT-1 and diffuse positivity for Chromogranin, Synaptophysin and NSE [7] (Table 1). Rhabdomyosarcoma is one of the differential diagnosis because it affects any age including children and adult and microscopic picture that show foci of pleomorphic and bizarre cells in addition to necrosis, calcification, nesting pattern and increased vascularity. But negativity for MSA, Desmin and Myogenin exclude this diagnosis [8] (Table 1). Although lymphoma may be considered because of the age and similarity to the gross picture as regards to the lobulation, necrosis, hemorrhage, microscopic picture of discohesive cells with vesicular nuclei and prominent nucleoli. However, it is rapidly excluded because of negativity of LCA and other lymphoid markers [9] (Table 1).

Considering PNET they are close entities and can affect adrenal gland with a slight more cases reported for PNET [10–14]. However, the presence of neuropil and calcification are against PNET, in addition ganglionic differentiation is very rare in PNET and of course the negativity for CD99 excludes any more possibilities for PNET [14] (Table 1).

Kidney is more commonly to be an adjacent site for neuroblastoms especially for cases arising in the adrenal gland and different studies reported neuroblastoma metastasis spreading to kidney [15,16]. According to Fishman et al., 2007 [17], the initial manifestation of stage IV neuroblastoma could be impaired kidney function which is explained by invasion of renal parenchyma with tumor cells obstructing renal tubules resulting in renal impairment. In our case, we have no evidences of primary tumor anywhere suggested by investigations, intraoperative data and lack of previous history of neuroblastoma or ganglioneuroblastoma, so, we considered the case of primary adrenal origin. In some cases, the primary origin of neuroblastoma is unknown [2]. Some investigators demonstrated the presence of neural crest cells in adrenal tissue as a source of neuroblastoma [18] and others determined the time of their arrival to the developed adrenal at 26–27 somite stage [19]. Neural crest cells were reported to colonize dorsal adrenal prior to ventral adrenal and they are the sole source of adrenal neurons and glia [19]. Long time ago, some authors believed that pancreatic islets cells were of neural crest origin [20] but currently it is proved to be of endodermal origin [21] and neural crest cells are required for beta cell maturation [19]. According to Kumar et al., adrenal may carry a supportive environment for neural crest derived neuroblasts and provide the developmental factors required for neuroblastoma progression [6]. Although the course of adult neuroblastoma may be longer compared to pediatric age group, however, the outcome is poor and this is reported previously [4,22]. The unfavorable histology of the poorly differentiated neuroblastoma may share in the fatal outcome of our case and other similar cases [23]. In addition, N-myc amplification was one of the molecular events associated with dismal prognosis [24] and unfortunately our patient may experience this amplification.

Figures

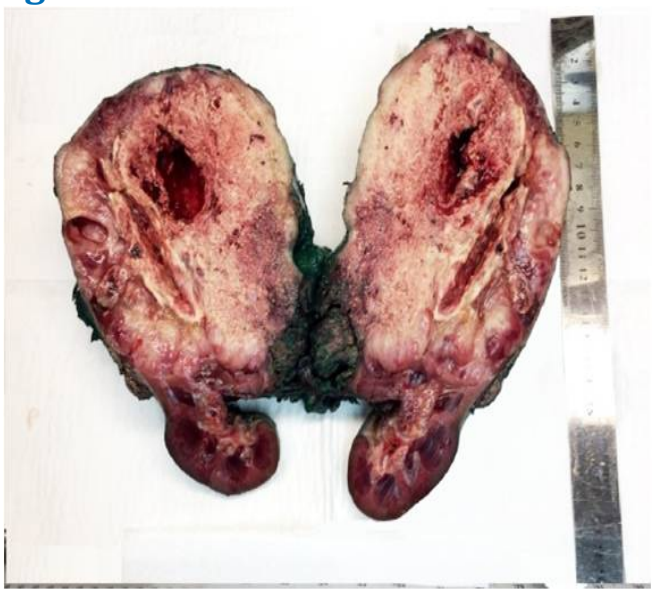

Figure 1: Gross image of the left kidney showing a mass, occupying the upper pole, tan white-yellow in color with areas of hemorrhage and necrosis with central cystic degeneration.

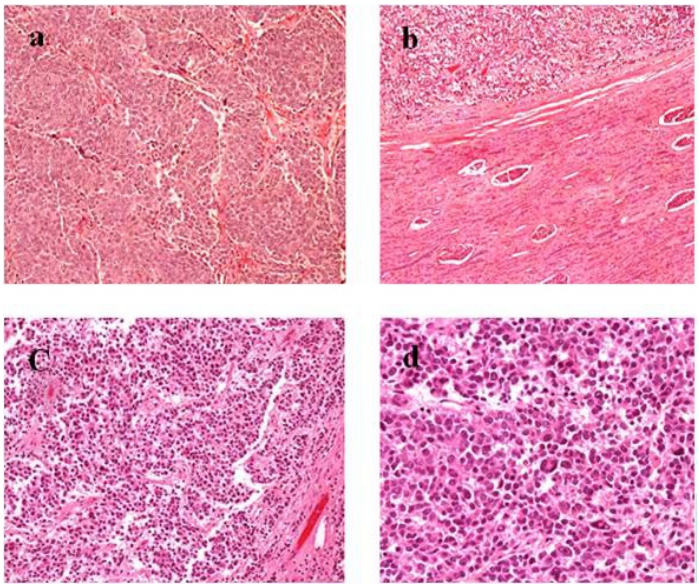

Figure 2: A) The neoplastic cells are arranged in nodules separated by fibrovascular septa. B) The neoplastic nodules are invading the adjacent kidney tissue. C & D) The tumor cells are small blue, arranged as vague nests entangled by neurofibrillary background with increased vascularity (Hematoxylin and Eosin stain).

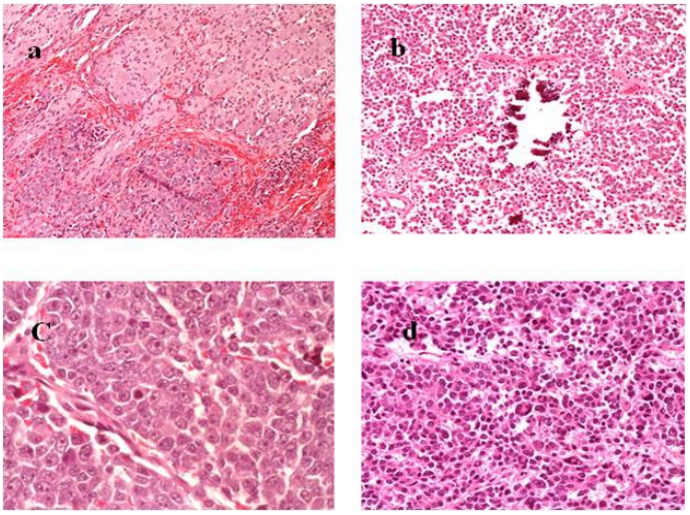

Figure 3: A) Areas of the tumor showing collection of ganglion cells. B) Calcification. C) Abnormal mitosis and prominent eosinophilic nucleoli. D) Tumor giant cell formation and bizarre cells (Hematoxylin and Eosin stain).

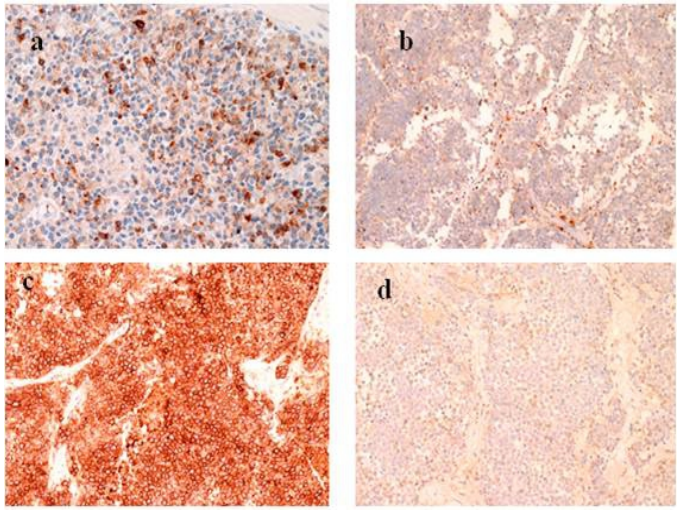

Figure 4: A) Strong positivity for chromogranin. B) S100 immunoreactivity in the stroma surrounding the tumor nests in neuroblastic areas. C) Strong and diffuse positivity for CD56. D) The neoplastic cells did not express CD99 (Immunohistochemical stain).

Tables

Table 1: The differentiation between the main five categories considered in the reported case as regards clinical, gross, microscopic and immunohistochemical data.

	Nephroblastoma (Wilms tumor)	Rhabdomyosarcoma	Lymphoma	PNET	Neuroblastoma
Age	Young	Any age	Any age	Young	Children but can occur in adult
Sex	Female	Male>	M:F ratio of 1.3:1	Male>female	
Site	Any part of the kidney	Mainly kidney	Kidney or adrenal gland	Any part of pancreas	Adrenal gland with extensive renal involvement is rare.
Nodularity or lobulation	Present	Absent	Present	Present	Rare
Size	Large	Small size not exceeding 5 cm	Large	Large	Large
Necrosis and hemorrhage	Present	Absent	Absent	Present	Present
Calcification	Present	Absent	Absent	Very rare	Present
Microscopic	Triphasic pattern consisting of blastema, stromal and epithelial components	Solid, trabeculae, glandular, gyriform, psudorosette, nests	Mixture of sheets of primitive, undifferentiated, round to spindle cells admixed with haphazardly arranged in a myxoid stroma	Small blue cells not associated with neuropil and ganglionic differentiation is very rare	Small blue cells entangled in neuropil and could be associated with ganglionic differentiation

Positive for	WT-1 and vimentin	Vimentin, MSA, desmin and myoglobin	LCA	20% express low molecular weight CK, CD99, CK-pan, LCA and NSE	Synaptophysin, chromogranin, NSE and CD56. S100
Negative for	Cytokeratin, LCA and NSE	Cytokeratin, LCA and NSE	Cytokeratin and NSE	CK-pan, LCA and NSE	CK, LCA and RCC

Conclusion

Despite the rarity of adrenal neuroblastoma as a primary site of origin, however it should be considered in the differential diagnosis of renal masses in children and young adult. Neuropil and ganglionic differentiation are helpful features to recognize neuroblastoma and differentiate them from other small blue cell tumors. The fatal outcome of pediatric neuroblastoma depends on the age and stage of the tumour, which have impact on mortality.

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