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Evaluation of Distribution and Frequency of Neuroblastoma in Children in Azzahra Hospital of Isfahan between 1996-2007 and 2 years Survival

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Abstract

Neuroblastoma is more frequent extra cranial childhood malignancy the goal of this study is evaluate pattern of neuroblastoma and 2 years survival in isfahan and comparison with others studies. The counted cases were 45 patients.25 of them were male (55.6%) and 20 of them were female (44.4%). Female/male ratio was 1.25. Primary sites of tumor in 32 patients were retroperitoan (71%), in 8 patients were posterior mediastineum 17.8%, in 3 patients were cervical 6.7% in pelvis 4.4%. In clinical manifestation the abdominal mass is predominant (17 patients 37.8%), abdominal pain in 6 patients 13.3%, abdominal distention in 2 patients (4.4%) fever in 6 patients (13.3%), cervical mass in 4 patients (6.7%), weight loss in 1 patient (2.2%). In evaluation of bone marrow biopsy 22 patient have metastasis to bone (48.8%) and 23 patients have not metastasis (51.1%). In evaluation of peripheral blood smear 29 patient have hypochrome RBC (64.4%) 32 patients have anisocytosis (71.1%), 30 patients have microcytosis (66.7%), 7 patients have low platelets (15.6%), 6 patients have high platelets 13.3%, 5 patients have lymphocytosis (11.1%), 7 patients have atypical lymphocyte (15.6%) 35 cases of them had died (77.8%), and 10 patients had been being alive (22.2%). Statistical analysis show us mean survival of patient with surgical process was 38.8 months and for patient without surgery was 30.6 months. Total 30 month survival in our study was 50%. Female/male ratio (1.25) in our study is same as other studies like a study in Saudi Arabia 53% of our cases was under 20 months 0.44% of them between 20-80 months 3% over 10 years as same result of others study. Retroperitoan is dominant primary site (71%) like other studies. But there is not significant relation between metstatic bone marrow biopsy and survival. Our result about prognosis (30 month survival was 50%) is less than other countries.

Keywords: Neuroblastom • Retroperitoan • Diagnosis

Introduction

The goal of this study is evaluation pattern of gender, age, clinical presentation, primary sites, peripheral blood smear and bone marrow biopsy and 2 years survival of patient with neuroblastoma in azzahra hospital of isfahan between 1996-2007 and comparison with past studies for facilitating of early diagnosis in low stage and increase survival of neuroblastoma in our country and making a basic information for future study in this field [1].

The neural origin of neuroblastoma was first poposed by virchow in 1984 and succeeding years brought a slow acquisition of understanding of the condition. Marchnd is credited with recognizing the similarity of neuroblastoma cells to cells of the sympathetic nervous system [2]. Neuroblastoma is a malignancy of neural crest cells it is more frequent childhood extracranial malignancy 30% of neuroblastoma occurs in first year 50% of them occur between 1-4 years only 5% between 10-14 years [3].

In recent study in 2009 each year 1500 cases occur in Europe and 700 in USA and Canada accounting for about 28% of all cancers diagnosed in Europe and US infants [4].

In recent years screening programmes have been implemented in parts of several countries, including Japan, Germany and Canada although programmes were associated with a vast increase in the incidence of stage 1 disease, there is little evidence of decrease in the incidence of late stage disease [5].

Some studies suggest different risk factors like genetic predisposition and prenatal age, socio -economic measures, parental occupational exposure, maternal alcohol consumption maternal recreational drug use, some drugs likes diuretic, contraceptives,

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radiation and ultrasound exposure but none of them are not confirmed [6]. In histological view the immature neuroblastoma are seen as sheets of dark blue cells with scanty cytoplasm set in a delicate vascular stroma [7]. Rosset formations consisting of a ring of neuroblasts around a neurofibrilary core, is a characteristic feature but is often absent [8].

Materials and Methods

Patient with neuroblastoma often come with sign and symptoms that indicated to primary sites of tumor because of 75% of neuroblastoma lcated in abdomen (25% in any sites in retroperitoan and 50% in adrenal) an abdominal mass is a dominat presentation, other sites are posterior mediastineum 20%, cervical 1%, pelvis 4% [9].

Some of clinical manifestations of neuroblastoma are:

1. **In head and neck:** Bilateral palpable mass, horner syndrome.
2. **In Eye and orbit:** Raccoon eye, encephalopathy, ptosis, palpebral and conjunctival edema, papillary edema, retinal hemorrhage, optical atrophy, opsoclonus.
3. **In cervical ganglion:** Hetrochromia, riditis, anisocoria, horner syndrome.
4. **In abdomen:** Abdominal mass, abdominal pain.
5. **In pelvis:** Urinary retention, constipation presacral mass.
6. **In para spinal:** Limping, hypotonia, paraplegia, scoliosis muscular atrophy.
7. **In lymph nodes:** Enlargement of lymph nodes.
8. **In bone:** Pain limping.
9. **In skin:** Blue berry muffin appearance.
10. **Paraneoplastic syndrome:** Flashing, paleness, headache, hypertension, palpitation, diarrhea.

Paraclinic finding

Several biochemical markers of disease are found in patient serum include Neuron Specific Enolase (NSE), Lactate Dehydrogenase (LDH) and ferritin [10].

Metabolite of catecholamines are found in urine of 90% of patient with neuroblastoma these catecholamines are Vanil Mandelic Acid VMA and Hemo Vanilic Acid HVA [11].

Simple x ray is a useful device for diagnosis of posterior mediastineal mass. Sonography is a first imaging evaluation in patient with abdominal mass but it is less sensitive and specific against CT and MRI. CT scan is a useful and usual imaging method for evaluation of neuroblastoma. MRI is most useful and sensitive imaging method for diagnosis and staging of neuroblastoma. MIBG scan (Metaiodo Benzyl Guanidine) is selective method for evaluation of bone and bone marrow envolvement. Bone Marrow Biopsy (BMB) is a routine and important way for detection of bone marrow involvement.

Treatment

The management of patient with neuroblastoma involves a multidisciplinary team. The composition of the team will vary different institution treatment modalities at present include chemotherapy, surgical intervention, and radiotherapy. These are provided in turn by pediatric oncologist, pediatric surgeons, and pediatric radiotherapists.

Prognosis

Prognosis of neuroblastoma is dependent to age and stage and biologic features of disease infant have best prognosis (5 years survival 83%), in 1-4 years 55%, in over than 4 years 40% the survival is not varies by gender and race.

This is a retrospective, and survival calculator study based on the patient's files with confirmed neuroblastoma diagnosis in azzahra hospital between 1996-2007 (under 15 years). This study was done by census method. Diagnosis of patient confirmed by report of pathology samples.

We prepared a check list which contained gender, age clinical presentation, primary sites, result of peripheral blood smear and bone marrow biopsy.

Period of this process is about 3 months from January 2009 to March 2009, then we entered gathering data from check list into software, analysis and report of the result was done by statistical methods. For calculation of 2 years survival we used telephone numbers and address of patient which register in their files.

Results

In our study 45 patients with neuroblastoma was assessed. Mean age of the 25 patients was male (55.6%), 29 patients was female (44.4%) female/male ratio is 1.25 mean age of male is 26.1 months and in female is 18 month (Figures 1 and 2).

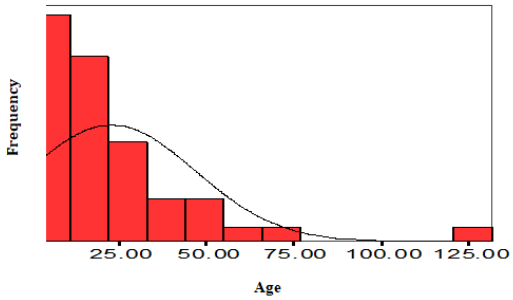

Figure 1. Distribution of frequency of patient with neuroblastoma according to age groups.

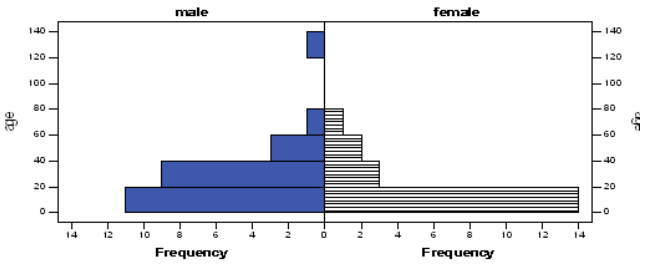

Figure 2. Distribution of frequency of age between two genders.

Primary site in 32 patients was retroperitoan (71.1%), in 3 patients was cervical (6.7%), in 8 patiens was posterior mediastineum (17.8%), in 2 patients was pelvis (4.4%) (Figure 3), (Table 1).

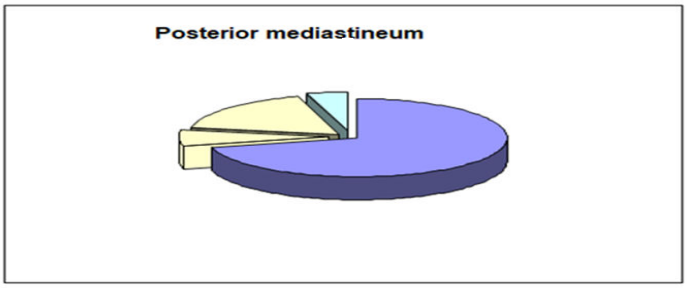

Figure 3. The percent of frequency of primary sites of patients. Note: Pelvis: 17/8%, Cervical: 6/7%.

Clinical manifestation in 17 patients was abdominal mass (37.8%) in 7 patients was movement disorder (15.6%), in 6 patients was abdominal pain (13.3%), in 2 patients was abdominal distention (14.4%), in 6 patients fever (13.3%) in 4 patients was cervical mass (8.9%), in 1 patient was weigh loss (2.2%), in 2 patient pulmonary sign and symptoms (4.4%).

Bone marrow biopsy in 22 patients was metastatic (48.8%), in 23 patient (51.1%) was not metastatic (Table 2).

In peripheral blood smear 20 patients have hypochrome RBC (64.4%), 32 patient have anisocytosis (71.1%), 30 patients have microcyosis (66.7%) 7 patients have low platelets (15.6%), 6 patients have high platelets (13.3%). 6 patients have lymphocytosis (11.1%), 7 patients have atypical lymphocyte (15.6%) (Table 3).

Total	Female		Male		Gender primary site	
	Numbers	Percent (%)	Numbers	Percent (%)	Numbers	
71.1	32	80	16	64	16	Retroperitoan
6.7	3	5	1	8	2	cervical
17.8	8	15	3	20	5	Posterior medistineum
4.4	2	0	0	8	2	Pelvis
100	45	10	20	10	25	Total

Table 1. Distribution of frequency of primary site of tumor in two genders.

Total	Female		Male		Gender BMB	
	Numbers	Percent (%)	Numbers	Percent (%)	Numbers	
48.9	22	45	9	52	13	Metastatic
51.1	23	5	11	48	12	Non-metastatic
100	45	100	20	100	25	Total

Table 2. Distribution of frequency of BMB in two genders.

P	Metastatic	Non-metastatic		BMB (-+)		
		Numbers	Percent (%)	Numbers		
0.048	78.3	18	50	11	+	Hypochrome
	21.7	5	50	11	-	
0.67	73.9	17	68.2	15	+	Anisocytosis
	26.1	6	31.8	11	-	
0.09	73.8	18	54.5	12	+	Microcytosis
	21.7	5	45.5	10	-	

0.24	21.7	5	9.1	2	+	Low platlets
	78.3	18	90.9	20	-	
0.41	17.4	4	9.1	2	+	High platelets
	82.6	19	90	20	-	
0.6	8.7	2	13.6	3	+	lymphocytosis
	91.3	21	86.4	19	-	
0.09	26.1	6	4.5	1	+	Atypical lymphocye

Table 3. Distribution of frequency of BMB in two genders and relation with peripheral blood smear.

Discussion

Mortality

35 patients (77.8%) had expired and 10 patients (22.2%) had been being alive. Mean age of alive person was 52.2 months, mean age of alive in patients with bone marrow metastasis was 57.6% and for without metastasis was 44 months, according to t test there is not significant differentiation between these two groups (p=0.32).

Survival

Mean survival from diagnosis to death is about 35 months, and median was 30 months in other language 30 month survival is 50%.

23 patients had been under surgery and 22 patients had not mean age of death in patients with and without surgery in order to 37.1 months and 27.6 months. According to t-test there is a significant differentiation between two groups (p=0.029).

Our statistical result reports mean survival for patient with surgery is about 38.8 months and for patient without surgery was 30.6 months according to log rank test the mean survival of these two group was significant (Figure 4).

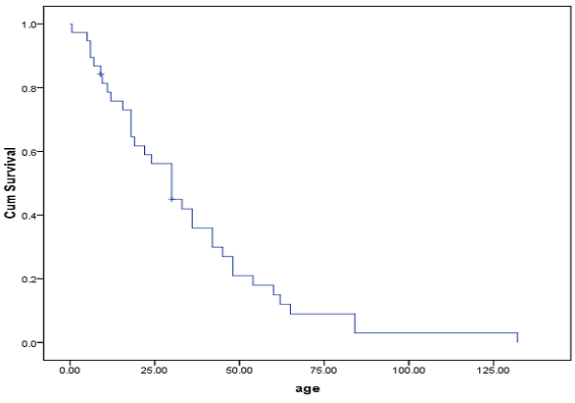

Figure 4. Diagram of kaplan-meier curve for survival of 42 patients. **Note:** – Survivial function, Censored

Conclusion

Our goal from this study was assessment of pattern of neuroblastoma in isfahan azzahra hospital and comparison with other studies and detection of 2 years survival. male/female ratio (1.25) as same as other studies like an study in Saudi Arabia 24 patients are under 20 months (53%) 20 patients were between 20-80 months (44%) 1 patient was over 10 years (3%). These result are in coordination with a result from a study in north America and a result from Europe.

About primary site of tumor in the patients with neuroblastoma 71% of tumors located in retroperitoan as mentioned in other studies like a study in Germany which 80% of tumors located in retroperitoan. In clinical manifestation abdominal mass is dominant in 37% of patients as mentioned in text book of pediatric surgery.

An important point is a relation between patient with hypochrome RBC and existence of metastases to bone marrow the hypochrome RBCs were found in 78.3% of patients with metastasis and only in 5% patients without metastase but there is not significant relation between metstatic bone marrow biopsy and survival. Our result about prognosis (30 month survival was 50%) is less than other countries.

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