
CASE REPORT

Neuroblastoma in a Newborn Infant

by

H. TJANDRA*, E. SARWONO* and E.H. TAMBAYONG**

(From the Department of Child Health, Medical School, Airlangga University/ Dr. Soetomo Hospital, Surabaya, Indonesia. **Department of Pathology, Medical School, Sam Ratulangi University/Gunung Wenang Hospital, Manado, Indonesia).*

Abstract

The incidence of neuroblastoma, one of the most common malignant neoplasms in infants and children, is greatest at the age of two years; but occasionally is diagnosed at birth. The diagnosis may be simple or very complicated. It is even more difficult when it occurs in the newborn infant. At this age the primary tumor is usually small and undetected. The presenting sign is generally due to the massive hepatomegaly caused by metastasis.

In this report we present a rare case of congenital neuroblastoma with the sole clinical manifestation of liver enlargement. The difficulties in arriving at a correct diagnosis are emphasized.

Introduction

Neuroblastoma, one of the most common malignant neoplasms in infants and children, mostly arises from the adrenal medulla, although it may originate from any site along the sympathetic chain. The incidence is greatest at two years of age but occasionally it is diagnosed at birth (Evans et al., 1976). The diagnosis may be a simple matter in some instances, while in others it is very complicated. Errors in diagnosis may be made by the experienced physician whether he be a clinician, pathologist or roentgenologist (Dargeon, 1963).

It is even more difficult when the neoplasm is present in the newborn infant. In a young infant, especially in a newborn, the primary tumor is usually small and remains undetected (Anders et al., 1973). The presenting sign is generally due to the presence of metastasis to the liver causing a massive hepatomegaly (Anders et al., 1973; Arey 1975; Schaffer and Avery, 1977).

This is a report of a case of neuroblastoma in a newborn in which liver enlargement was the sole clinical manifestation and it is believed to be the first in our hospital. We consider the case worth reporting from the fact that it is unquestionably a congenital form which is sufficiently rare to warrant attention.

Case report

On March 12, 1978, a 2950 gm and 47 cm long female infant was born by normal delivery to a healthy 34-year-

old Indonesian woman after about 37-week pregnancy. The Apgar score was 2 at one minute and 4 at five minutes. Resuscitation was done immediately after birth. The mother's history and physical examination were not remarkable and the present pregnancy had been normal until the onset of labor. Except for vitamins, no drug was taken by the mother during her pregnancy. There were no miscarriages, stillbirths, or premature labor. The mother made an uneventful recovery. Pathologic gross examination of the placenta was negative.

The infant was transferred to the Neonatal ward of the Child Health Department, Medical School, Sam Ratulangi University/Gunung Wenang Hospital Manado, from the delivery room of the same hospital. Physical examination revealed a term infant with a very distinct abdominal mass. The baby was rather weak, a little dyspneic but neither icteric nor cyanotic. Respiration rate was 48/minute, regular; pulse rate 138/minute, regular. Rectal temperature was 36.8 degrees Centigrade. No particular findings were found on the heart and lungs. A very distended and glistened abdomen was noted.

A firm tumor with smooth surface, filling almost the whole abdominal cavity, was palpable. Routine blood examination showed Hb conc. 14 gm%, leucocyte count: 19,500/ml., and thrombocyte count: 275,000/ml. The abdominal enlargement was clinically regarded as resulting from pronounced hepatomegaly. Radiographic study indicated a

marked enlargement of the liver and spleen with downward displacement of the intestines. Clinically we were only able to differentiate some of the common causes of liver enlargement in the newborn infant:

1. Primary tumor of the liver.
2. Fetal erythroblastosis.
3. Congenital syphillis.
4. Gaucher's disease.
5. Metastasis from a neoplasm.

Parenteral administration of a 10% Dextrose solution was given. The infant was referred to the Surgical Department, but died before she was examined by the surgeon, exactly 28 hours after birth. Laboratory examination and biopsy in the attempt to differentiate the above-mentioned diseases were never done. At the end of the first day of life the infant was cyanotic, the pulse rate increased from 138/minute to 160/minute, and the respiration from 48/minute to 58/minute. These continued increasing up to 170/minute and 72/minute respectively. The pulse became feeble and the respiration irregular. The baby looked edematous around the eyes and the extremities. Her condition deteriorated and finally succumbed.

Retrospective study of the fluid administration chart showed that during the patient's life (28 hours) the fluid given has amounted to 325 ml, while the amount initially planned was 245 ml (70 ml/kg b.w./day), that means 80 ml more than what she should have received.

Severe asphyxia which itself may lead to cardiac enlargement, excessive fluid given combined with the clinical condition in the last few hours of life led us to assume that cardiac failure due to severe asphyxia and overhydration brought the infant to her death. However, it was regretful that chest X-ray was not done to substantiate this evaluation.

Autopsy revealed a massively enlarged liver weighing 600 gm and measuring 18 cm in its greatest diameter, almost covering the whole abdominal cavity. The consistency was firm. Its reddish brown surface was smooth and studded with numerous grayish white nodules diffusely scattered all over. The same pattern was observed on the cut surface.

No abnormalities was found of the retroperitoneal sympathetic chain. Microscopic examination showed a liver tissue consisting of groups of undifferentiated tumor cells with a uniform, rounded and hyperchromatic nuclei and scanty ill-defined cytoplasm, arranged in a rosette/pseudorosette structure. The same picture has also been found in the adrenal medulla of both the suprarenal glands which surprisingly did not show any enlargement. Each weighed 3.5 gm and measured $2 \times 0.75 \times 1.5$ cm. The histologic diagnosis was primary adrenal neuroblastoma with metastasis to the liver. The kidney and the pancreas only showed hyperemia without any evidence of metastasis. The spleen was also normal. Edema of the lung was noted on gross

as on microscopic examinations, without any sign of metastasis.

Family data : the patient was the tenth child of 10 children. All siblings were in good health and showed no physical abnormalities on examination except the first and the third children who died of gastroenteritis at the age of 6 and 1½ years respectively. The paternal great grand father was an alcoholic and died of a disease other than malignancy.

The 36-year-old father and 34-year-old mother had no pertinent ailments. All the brothers and sisters of the father had died at the age below 5 years old of unknown causes. The mother had only one sister who was in good health. The family cooperated only in the initial phase of the epidemiologic study but later refused any further investigation. Otherwise we would like to examine more deliberately all the families and close relatives physical as well as laboratory which might inform us about any association pertaining to the patient's disease.

Discussion

Neuroblastoma is a rapidly growing and malignant neoplasm. It is the most common tumor in the first decade of life, and yet it is relatively rare at birth (Birner, 1961; Evans et al., 1976; Falkenburg and Kay, 1953; Larimer, 1949; Strauss and Driscoll, 1964). However, among fetal and neonatal malignancies its incidence is higher than any other tumors (Anders et al., 1973). In some cases, the tumors were known to have caused dystocia (Hagstrom, 1930) and

have ever been reported in a stillborn fetus (Birner, 1961).

A neoplastic growth consisting of neuroblastoma, ganglioneuroma and fibroncuroma in a stillborn fetus has also been reported by Potter and Parrish (1942). Sexes differ little if any at all (Willis, 1953).

In newborn infants, the adrenal gland is the most frequent site of origin, most 30 - 50% (Birner, 1961; Evans, and Glass, 1976; Willis, 1953). Right and left adrenals appear to be about equally affected (Willis, 1953). Scott et al., in 1953 suggested that right sided adrenal neuroblastoma occurs at earlier ages than the left sided one. They have also reported the occurrence of bilateral adrenal neuroblastoma. In our case both the adrenals were the site of the primary tumor. Interestingly enough they were not enlarged.

In his study, Dargeon (1963) concluded that no familial occurrence has been recorded, and Willis (1953) stated that neuroblastoma shows no hereditary or familial tendency. In contradiction with these, Wagget et al. in 1973 reported neuroblastoma in 2 sib pairs. Chatten and Voorhess (1967) discovered 4 of 5 siblings in one family having neuroblastomas. They suggested that some neuroblastomas may be inherited. Leape et al. (1978) also reported multifocal nondisseminated neuroblastoma in 2 siblings, and considering the familial characteristic of this kind, were of the opinion that evaluation of every other family of the patient is mandatory.

None of the nine siblings of our patient and her close relatives seemed to have the disease, but we did not know about the siblings of the father who had died at young ages of unknown causes. Sherman and Roizen (1976) and Pendergrass and Hanson also in 1976 discovered infants born to women whose medication included dilantin throughout pregnancy, developing neuroblastoma. The history of taking the drug and other drugs or traditional herbs except vitamins during her pregnancy, was denied by our patient's mother.

A wide variety of congenital anomalies associated with neuroblastoma has been described by many authors though there has been no special pattern to these occurrences (Chatten and Voorhes, 1967, Willis, 1953). Among the malformations identified were cleft lip and palate, microcephaly, hydrocephalus, PDA, aganglionosis etc. In our case no such malformations was noted.

Pepper syndrome is an adrenal neuroblastoma with secondary disease of the liver. Hepatic metastasis from intraabdominal neuroblastoma is not uncommon in neonates (Hendren, 1963). The primary lesion is usually small and remains undetected. The tumor is recognized by the liver metastasis, and hepatomegaly is likely to be the presenting sign (Anders et al. 1973; Schaffer and Avery, 1977; Willis, 1953).

In cases of neuroblastoma in the newborn the enlargement of the liver is most striking (Birner, 1961). Neuroblastoma

must therefore always be borne in mind in the diagnosis of hepatomegaly at birth. Congenital neuroblastoma simulating fetal erythroblastosis has been reported (Anders et al. 1973; Falkenburg and Kay, 1953). But in the latter, jaundice almost always appears in the first few hours of life or some times later. There is also puffiness and edema of the extremities. The diagnosis can be confirmed by blood examination of both the mother and the baby. Congenital syphilis shows an early sign of snuffles. The nose becomes obstructed and begins to discharge, the lips thickened roughened and tend to weep. Besides hepatomegaly and splenomegaly, general glandular

Dark field examination from the skin lesion will confirm the diagnosis.

Inborn errors of lipid metabolism like Gaucher's disease, also shows splenomegaly

infant is lethargic and feeds poorly. Xanthomas are usually present on the eyelids or elbow of the newborn. A marked elevation of plasma cholesterol and moderate increase of triglyceride are of diagnostic importance. Physical signs and symptoms characteristic

mentioned diseases were not found in our patient. The possibility of a primary liver tumor like hepatoblastoma should also be considered, notwithstanding the statement of Singh et al. (1978) that secondary deposits in the liver is 25 times more common than primary liver cancer. Clinical differentiation between these two is quite difficult. Histologic exa-

mination seems to be the only solution for this.

The presence of blanching subcutaneous nodules may represent a new diagnostic sign characteristic neuroblastoma (Hawthorne et al. 1978). However not all neuroblastomas in the newborn always show cutaneous metastasis which gives the blanching phenomenon. Our patient did not show any evidence of this sign. Not infrequently the diagnosis of neuroblastoma in a newborn is indeed difficult rather than easy. It has been stated by Dargeon (1963) that the diagnosis may be a simple matter in some cases while in others the diagnostic difficulties of the clinician, radiologist and surgeon may not be solved even by necropsy.

This is exactly what happened with our case. The diagnosis was only possible retrospectively after autopsy had been done and yet in arriving correct diagnosis, still many difficulties were encountered. Clinically we could only make a differential diagnosis of enormous liver enlargement.

But before further examinations could be done the patient died. Fortunately an autopsy was consented by the parents.

Microscopic examination at first resulted in the diagnosis of hepatoblastoma. But this was doubted by the Department of Pathology, Medical School, Airlangga University, Surabaya, which considered neuroblastoma more likely. Adrenal neuroblastoma with liver metastasis was finally confirmed after consul-

tation with the Department of Pathology, Medical School, University of Indonesia, Jakarta.

According to Evans and Glass (1976) and Schaffer and Avery (1977), metastasis to the liver is far more common in the neonate, while bone and lung metastasis are uncommon in this period (Birner, 1961; Schaffer and Avery, 1977).

Especially in those cases with massive liver enlargement due to metastasis, no metastasis has been observed in the lungs (Willis, 1953). The liver enlargement in our case was considered as a metastasis of a primary adrenal neuroblastoma, and no lung metastasis was detected. Metastasis to the placenta has been reported by Anders et al. (1973) and Strauss and Driscoll in 1964. As we did not expect the disease, deliberate examination of our patient's placenta was not done.

This was verified by Strauss and Driscoll (1964) who stated: "A congenital malignant neoplasm is rarely suspected at birth, and the placenta is not always subjected to detailed examination".

In Bond's opinion (1976) neuroblastoma is an extremely unpredictable form of malignancy. Most interesting point discussed is the possibility of an initially neuroblastoma growth undergoing maturation and loss of malignancy with the passage of time. A congenital neuroblastoma undergoing spontaneous regression has been observed by Brett, et al. (1964). They considered the younger the age of

onset, the more likely is such regression to occur. In contradiction with Willis (1953) who considered that Pepper syndrome present at birth or appearing during infancy was usually fatal, Evans and Glass (1976) were of the opinion that the prognosis in the neonate was generally better than that in older children. Schaffer and Avery (1977) even considered it as remarkably good. Our patient succumbed exactly 28 hours after birth.

Retrospective analysis of the baby revealed clinical signs of heart failure which might be due to severe asphyxia at birth and fluid overload. This was substantiated by the findings of lung edema on necropsy.

Surgery, radiation and chemotherapy, alone or in combination are applied in the treatment of neuroblastoma depending upon the age, the stage and metastasis etc. Complete extirpation, when no demonstrable metastasis is present, is the treatment of choice (Evans and Glass, 1976; Arey 1975).

The response to chemotherapy is often dramatic, with the most impressive

results occurring in children under the age of one year (Schaffer and Avery, 1977), Evans and Glass (1976) were of the opinion that aggressive attitude toward treatment was necessary in the neonate with this tumor even when it cannot be removed completely surgically or when there is metastasis. Evans et al., (1976) however, had a different opinion that since babies have an excellent prognosis, for them aggressive multimodal therapy can be more dangerous than the disease itself.

This was also suggested by Schwartz, et al. (1974) that the complication of therapy must be considered very carefully in those who have a good prognosis including infants. Since the correct diagnosis of our patient was not established during her life, no appropriate treatment could be given.

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