

A Severe and Rapidly Progressive Case of Proteus Syndrome in a Neonate Who Presented with Unilateral Hydrocephalus Apart from Other Typical Features of the Proteus Syndrome

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ABSTRACT

Proteus syndrome is a rare hamartomatous disorder affecting multiple tissues and manifesting itself in a variety of ways. The understanding of the complete spectrum of clinical features, the natural clinical course of the disease and the proper management of such a rare but highly variable syndrome depend heavily on experiences gathered by previously reported cases. We present an unusually severely affected and rapidly progressive case of proteus syndrome in a neonate who presented with craniofacial hemihypertrophy, subcutaneous masses, capillary hemangioma, varicose veins, epidermal nevi and macrodactyly. The cranial ultrasonogram revealed unilateral hydrocephalus with partial obstruction of the foramen of monro.

Key words:

Craniofacial hemihypertrophy, proteus syndrome, unilateral hydrocephalus

INTRODUCTION

First description of Proteus syndrome (PS) dates back to 1979 when Cohen and Hayden described two patients of this syndrome.^[1] It was termed by Wiedemann et al in 1983 as PS after the Greek God Proteus who could change his shape at will to avoid capture, emphasizing the variability of clinical expression of the disease.^[1] Several central nervous system malformations (CNS) have been described to be associated with PS in individual cases. The multiple, diverse, somatic manifestations of the syndrome evolve over time and the patients are usually asymptomatic or only partially affected in the neonatal period. The purpose of this article is two fold: (1) To present an unusually severely affected and rapidly progressive case of PS, who presented in the neonatal period with all the typical features of the syndrome (2) To report a new possible association of PS in the form of unilateral hydrocephalus.

CASE REPORT

A 5-day-old male baby presented with enlarging head size and multiple physical abnormalities. He was the first child of nonconsanguineous parents. The pregnancy had been uneventful. He was born by caesarean section with birth weight of 2600 gm (5th centile), length 50 cm (50th centile), and head circumference 38 cm (>90th centile). The baby was on breast feeds. There was no relevant family history.

On physical examination, the baby had marked right-sided hemihypertrophy involving face and cranium. The facial

hemihypertrophy included enlarged palpebral fissure, cheek, ear, and lip [Figure 1]. There was marked wasting of subcutaneous tissue of arms and thighs on both sides. Capillary hemangioma large in size was present in both flanks. There was venous prominence over scalp and trunk. Multiple subcutaneous masses were palpable over both thighs clinically appearing to be lipomas. The second and third toes of the left foot were significantly enlarged [Figure 2]. The head circumference has increased to 39.2 cm (95th centile).

A cranial ultrasonogram (USG) was carried out which revealed selective dilatation of the right ventricle with partial occlusion of the right foramen of monro [Figure 3]. The brain parenchyma, left lateral ventricle, corpus callosum and cerebellum were normal. The cranial USG finding together with rapidly increasing head circumference in our patient indicated toward right-sided unilateral

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hydrocephalus. Computed tomography of the head was advised to confirm the USG finding and to detect any other associated CNS anomalies. But the baby became lethargic on day 7 of life. He developed marked respiratory distress. Examination revealed a bluish discoloration over anterior trunk and a large venous prominence visible over left side of chest and abdomen originating from mid axillae with flow from upward to downward [Figure 4]. The platelet count was $30 \times 10^3/\mu\text{l}$. Other parameters of hemogram and sepsis screen were normal. Duplex scan of chest and abdomen was advised but the baby died before the investigation. Parents refused to go for autopsy.

DISCUSSION

PS is a rare, sporadic, complex, congenital, sometimes lethal hamartomatous disorder characterized by a variety of malformations and disproportionate, asymmetric overgrowth of multiple tissues.^[1-3] The typical clinical features include hemihypertrophy, macrodactyly,

subcutaneous tumors, lipolyphohemangiomas and epidermal nevi.^[1-3]

The patients of PS are usually asymptomatic with no any gross abnormality detectable at the time of birth.^[1] As the child grows older, characteristic manifestations of the disease appear suggesting progressive nature of the disease. The presence of many characteristic features of the disease at the time of birth in our patient suggests that the clinical course of the disease can be progressive prenatally.

Most authors suggest that PS results from mosaicism for a mutation that is lethal in nonmosaic state. Recently, a somatic activating mutation in *AKT1* has been found in cases of PS, proving the hypothesis of somatic mosaicism.^[2] An early postzygotic mutation would be expected to present with more severe disease, because an early somatic cell carrying mutation would give rise to more abnormal cell lineages.^[3] This could explain the severity and rapid progression of the disease in our case.



Figure 1: Facial hemihypertrophy



Figure 2: Macrodactyly of second and third toe



Figure 3: USG cranium showing dilatation of right ventricle and partial obstruction of foramen of monro



Figure 4: Venous prominence over abdomen

The CNS malformations described to be associated with PS include hemimegalencephaly, hydrocephalus, corpus callosal abnormalities, Dandy Walker malformation, periventricular heterotopias, cysts, and neoplasm like meningioma and pineoblastoma.^[1,4]

The disproportionate asymmetric overgrowth characteristic of PS can involve one half of the body (hemihypertrophy) or a limb or a digit (macroductyly). Hemihypertrophy can be partial or complete. The partial hemihypertrophy involving the skull and face present as craniofacial asymmetry. The craniofacial asymmetry was present in previously reported cases and it was seen to be associated with hyperostosis of facial bones and calvaria, hemimegalencephaly and craniosynostosis.^[1] In our case, it was associated with unilateral hydrocephalus.

Unilateral hydrocephalus, a rare entity in itself, has been defined as the progressive dilatation of one lateral ventricle due to abnormal circulation of cerebrospinal fluid. The obstruction of foramen of monro is the most common cause. The foramen of monro can be obstructed by congenital atresia or stenosis, or morphological obstruction due to hemorrhage, neoplasm, gliomatous or vascular anomalies or intrauterine infections like mumps.^[5] Various neoplasm and cerebrovascular malformations has been described in previously reported cases of PS.^[4,6] On the basis of extensive vascular malformations present in our case, we think antenatal hemorrhage could be the most probable cause of obstruction of the foramen of monro, though hemorrhagic cast was not present in the ventricles in cranial USG.

Diagnosis of PS is primarily clinical. Because of the varied morphology of the patients, diagnostic criteria have been laid down.^[1] The closest differential diagnosis of this case is CLOVE syndrome, a newly delineated syndrome characterized by congenital lipomatous overgrowth, vascular malformations and epidermal nevi.^[7] The overgrowth in CLOVE Syndrome is congenital, as in our case. But the overgrowth in CLOVE Syndrome is of ballooning nature, proportionate and symmetrical, unlike PS where it is characteristically disproportionate and asymmetrical, as in the present case.^[7] Other differential diagnosis particularly in cases associated with craniofacial hemihypertrophy includes Haberlund Encephalocraniocutaneous Lipomatosis, Beckwith- Wiedemann syndrome, Hemifacial hypertrophy of Rowe, Bannayan syndrome, Klippel-Trenaunay-Weber syndrome and Mafucci syndrome.^[8]

Sudden death, as in our case, but in older age group has been reported previously and the usual cause was pulmonary thromboembolism, which is a recognized complication of PS.^[9] Functional ability and longevity in cases of PS vary with the severity of cutaneous and CNS abnormality.^[3,8] The full-blown picture of PS present in our patient since birth and his early death, suggest that children with normal infancy or fewer findings in early life may have an improved prolong survival. Limb anomaly like macroductyly and cranial anomaly like unilateral hydrocephalus or hemihypertrophy can be diagnosed in antenatal period itself by an obstetric USG and if found together in a patient may be highly suggestive of PS.^[5,10] The prenatal diagnosis of PS in severe cases by antenatal USG will lead to early diagnosis and proper management of this syndrome and its complications, and this may result in favorable clinical outcome.

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