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Hemangioblastoma: An Uncommon Cause of Polycythemia in a Child

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ABSTRACT

Polycythemia is a rare condition in children. Myeloproliferative neoplasms, including polycythemia vera although rare, is an important cause of childhood primary polycythemia. Secondary polycythemia is more common in children due to conditions causing hypoxia or due to pathologic erythropoietin production in malignancies like renal cell carcinoma, Wilms tumor or Hepatocellular carcinoma. Central nervous system hemangioblastoma is one of the rare causes of polycythemia. We report a 13-year-old girl with primarily neurological symptoms identified to be polycythemic during routine evaluation. Clinical examination and neuroimaging subsequently confirmed an intracranial space occupying lesion which was excised. Hemoglobin level normalized after tumor excision. This case report emphasizes the need for thorough systemic evaluation including central nervous system examination in children identified to be polycythemic.

Keywords: CNS tumor; hemangioblastoma; polycythemia

INTRODUCTION

Absolute erythrocytosis is defined by red cell mass >25% above the mean predicted value.[1] Although neonatal polycythemia is encountered frequently, it is rare in pediatric age group. Childhood polycythemia is usually secondary to cyanotic congenital heart disease. Primary erythropoietin independent erythrocytosis and polycythemia vera are uncommon causes of polycythemia in children. Polycythemia has been associated with erythropoietin secreting benign and malignant tumors of kidney, liver or adrenal gland. [1] Cerebellar hemangioblastoma is a rarer cause of polycythemia.[2]

Here, we report a case with progressive neurological symptoms who was identified to be polycythemic during laboratory evaluation.

CASE REPORT

A 13-year-old premenarchal female presented with complain of progressive headache and dizziness for 9 months to Tribhuvan University Teaching Hospital OPD after multiple consultations elsewhere. She also reported progressive loss of vision associated with occasional episodes of vomiting. Additionally, she also reported difficulty in speaking with slurred speech for preceding 2 months prior to presentation to this hospital. A total of 5 kg weight loss was documented over the span of 9 months. She was evaluated in different health centres for headache and dizziness which were treated symptomatically. With onset of visual blurring, she was evaluated by physicians who identified hypertension and started her on antihypertensives. Routine laboratory evaluation during this time identified polycythemia that prompted referral to this hospital. Review of her older records also revealed elevated hemoglobin concentration which had not been previously considered significant.

At presentation to this hospital, she was hypertensive (140/100 mm Hg) and appeared flushed with dark red hue in palpebral conjunctiva, oral cavity and her palms. She was fully alert and oriented with normal vital signs. She had relatively fluent speech and could describe her history herself. Her visual acuity was 1/60 bilaterally

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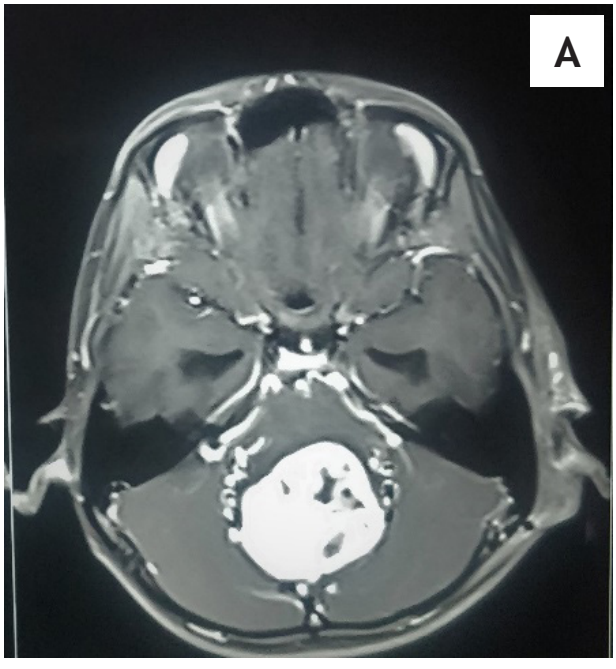
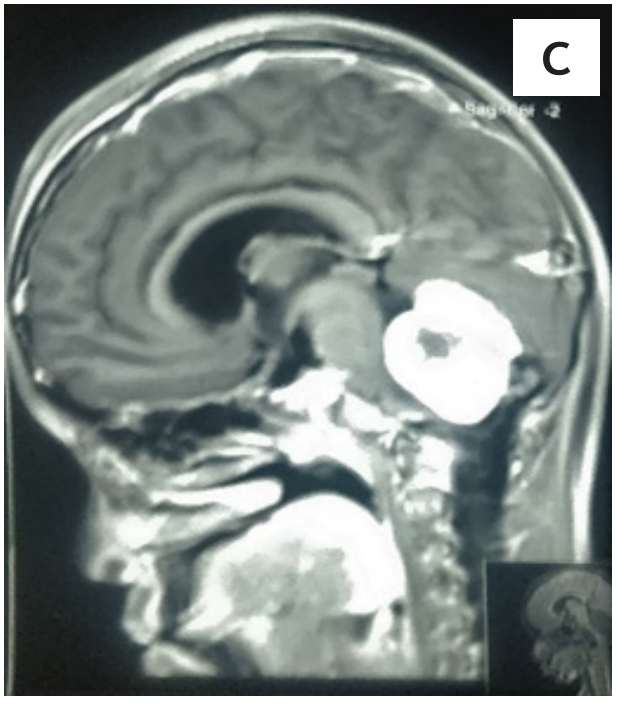
although prominent nystagmus and anisocoria were evident. Fundoscopy revealed bilateral disc edema. No other cranial neuropathy was identified. Motor examination was unremarkable except for an ataxic gait. Lymph nodes were not palpable and she did not have any intra-abdominal masses or organomegaly. No other abnormality was detected in systemic examination.

On the day of admission, her hemoglobin was documented as 20.2 gm/dl (hematocrit of 62.9%) with platelet count of 2,56000/mm3 and white cell count of 7860/mm3. A peripheral blood smear did not reveal any abnormal appearing cells. Her liver function and renal function tests were within normal ranges.

A brain MRI was performed which revealed a relatively well defined intensely heterogeneously enhancing intraventricular mass, approximately 4.9 X 4.5 X 3.5 cm in the floor of 4th ventricle seemingly arising from vermis with upstream hydrocephalus and mass effect on pons. (Fig 1,2,3). Emergency ventriculo-peritoneal shunting was done followed by complete tumor resection after 1 week. Subsequent histopathologic report of the excised tumor revealed proliferation of capillary admixed with abundant stromal cells which appeared as sheets of cells with abundant vacuolated cytoplasm suggestive of WHO grade 1 hemangioblastoma. Her hemoglobin returned back to normal (11.1 gm/dl) after a week of excision of tumor and remained in normal range during follow up. She remains symptom-free with improved vision and without residual neurological deficits during her last follow up 6 months after the surgery.





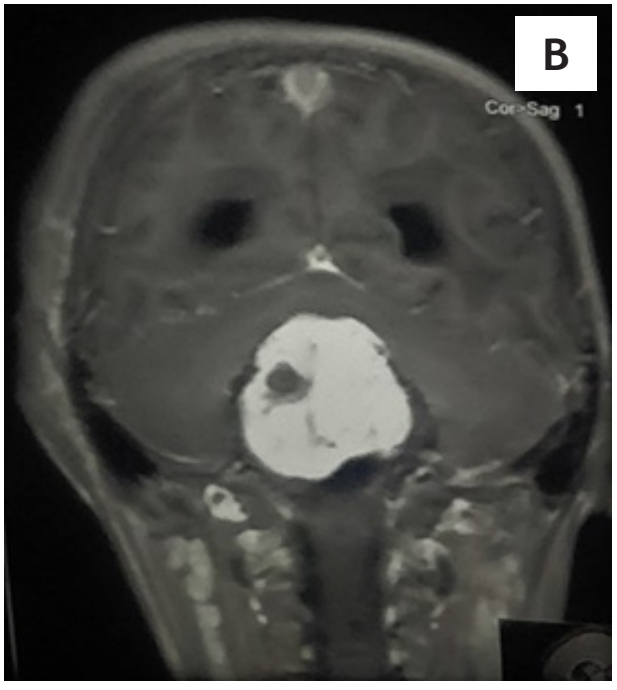


Figure 1. MRI head T1 (A)Axial (B)coronal (C)sagittal contrast images show well-defined heterogeneous and avidly enhancing lesion is seen in midline occupying the fourth ventricle with mass effect to pons. Proximal dilatation of temporal and occipital horns of bilateral lateral ventricles i.e obstructive hydrocephalus are seen in figure A and B caused due to mass at fourth ventricle.

DISCUSSION

Polycythemia constitutes an extremely rare group of diseases among pediatric patients and there are limited publications on pediatric polycythemia in South Asia. This case report nonetheless demonstrates importance of occasional rare causes of secondary polycythemia in children. Although mild polycythemia is relatively common in people residing in high altitudes in Nepal, this case report highlights the importance of thorough evaluation of patient should such laboratory report is identified.

The common causes of secondary polycythemia beyond neonatal period are chronic hypoxia due to high altitude, chronic lung disease or cyanotic congenital heart disease. Renal diseases like renal cyst, hydronephrosis or renal artery stenosis may also be the causes of erythrocytosis.[3] Polycythemia has been associated with benign and malignant tumors that secrete erythropoietin like nephroblastoma, renal cell carcinoma or pheochromocytoma.[3] Polycythemias may go unnoticed until it produces symptoms. In this case, patient had headache, dizziness and visual difficulties which had been attributed to uncontrolled hypertension without a definitive diagnosis of secondary cause for hypertension. Secondary cause of hypertension is common in children at this age and should prompt extensive search before a diagnosis of essential hypertension is made. Hyperviscocity caused by polycythemia can also lead to similar manifestations and should be particularly considered if a hemogram reveals increased red cell mass.

Some rare causes of polycythemia in children are primary familial and congenital polycythemia (PFCP) due to mutations of the erythropoietin (Epo) receptor gene and the myeloproliferative disorder polycythemia vera.[1] CNS malignancies like hemangioblastoma and meningioma may lead to polycythemia but cerebellar hemangioblastoma leading to polycythemia are more commonly reported in adults[4] and rarely in children. .

Hemangioblastoma are benign vascular tumors that arise from embryonic remnants of mesodermal origin, trapped in nervous system, during first trimester of life. Hemangioblastomas can occur sporadically or associated with von Hippel-Lindau disease, an autosomal dominant neoplastic syndrome that affects multiple organ systems. Hemangioblastomas are rare tumors in pediatric age group with an incidence less than 1 per 1,000,000.[5] The most common site is the cerebellum followed by spinal cord and brainstem.[6] Although a benign tumor, this tumor may be associated with lifelong neurological deficits based on its location and due to tendency to recur following excision.

Association between hemangioblastoma and polycythemia has been reported in case reports[2,4] and series.[7]The causative mechanism of polycythemia in hemangioblastoma is not entirely clear. Among different possible mechanisms, extramedullary hematopoiesis within the tumor, secretion of erythropoietin or other hematopoietic factors by the tumor are the most plausible explanations. Upregulation of erythropoietin production has been reported in cerebellar hemangioblastomas and renal cell carcinomas.[8] Loss of function mutation of VHL^{R200W} can also cause erythrocytosis in some tumors.[9]

In Nepal and South-Asian countries, there is a higher prevalence of anemia in children compared to the global and western countries, especially in adolescents and females. Due to this reason, interpretation of blood investigations is generally focused on exclusion of anemia and elevated hemoglobin may be not get equally important attention of the physician. If polycythemia had not been ignored in this case, detailed neurological evaluation in context of hypertension could have alluded the diagnosis much earlier.

Surgical excision is the primary treatment of choice for symptomatic CNS hemangioblastoma. Stereotactic radiosurgery is effective and safe method in adults with recurrent or multiple tumors, however there is limited data in children.

Similar cases have been reported by So et al[10], Samuel et al[6] and Kuhne et al[3], where patients had polycythemia and hypertension at the time of admission and were later diagnosed to have hemangioblastoma. In these case reports, the hemoglobin level normalized after complete excision of the tumor, which was similar to the course of events in this case. However, all these cases were exclusively reported in non pediatric age group. The presentation in our case in unusual in regards to pediatric population, where polycythemia is not a common clinical presentation of hemangioblastoma.

CONCLUSIONS

Hemangioblastoma is a rare cause of secondary polycythemia in children. This case highlights how a detailed history and clinical examination combined with basic laboratory investigation can provide clues towards an uncommon diagnosis in children. Children presenting with erthrocytosis should be evaluated in great detail for rare causes if common conditions producing polycythemia

are not identified.

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