Pheochromocytoma Presenting with Headache, Panic Attacks and Jaundice in a Child

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SYNOPSIS

Pheochromocytomas can mimic many unrelated diseases due to their various presenting signs; they are encountered very rarely in childhood. Recently, their neuropsychiatric aspects have become a subject of interest for many workers, but most of the findings reported previously have been observed in adults. We present a case report which is unique in that it concerns a child with pheochromocytoma and psychiatric findings consisting of depression and panic disorder, which were interpreted as being directly related to, since they disappeared after the removal of, the tumor. Depression was persistent and accompanied by a constricting-type headache, while panic disorder was acute and accompanied by a migraine-type headache. Another intriguing complication encountered in our case was jaundice; we considered that it could possibly have been due to an adverse effect of catecholamines on hepatocyte function. We conclude that a pheochromocytoma can be confused with neuropsychiatric disorders in children as well as in adults and that it should be considered in the differential diagnosis of such disorders.

Key words: pheochromocytoma, childhood, psychiatric.

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Pheochromocytomas are tumors arising from the chromaffin cells of the sympathoadrenal system. They can occur in all age groups, showing a peak incidence in the third to fifth decades and presenting very rarely in childhood. Nonfunctioning tumors have been reported, but most pheochromocytomas produce catecholamines and are associated with various signs and symptoms. Findings pertaining to their neuropsychiatric effects are being recognized with increasing frequency and have become a topic of interest for many researchers due to their surprisingly broad spectrum, which ranges from light-headedness to convulsions or dementia and from depression to paranoia. Pheochromocytomas are notorious for this extreme variability in clinical presentation, which can lead to considerable difficulty and delay in diagnosis; some clinically unsuspected tumors have been discovered during operations performed for abdominal pain and/or masses, or at autopsy.

Although abdominal pain appears to be a relatively common manifestation, we have not encountered a report of jaundice complicating pheochromocytoma in the previous literature.

We report a child presenting with headache, depression, panic attacks, abdominal pain and jaundice accompanying a right adrenal pheochromocytoma, with the hope of contributing to the knowledge of chromaffin-cell tumors.

CASE REPORT

A 15-year-old girl was referred for investigation of right subcostal pain, nausea, vomiting and jaundice. She had been evaluated 6 months previously at another hospital for headache that had started acutely, accompanying fever, tachypnea, confusion, agitation, prominent neck stiffness and slight cerebrospinal fluid pleocytosis had led to a clinical diagnosis of bacterial meningitis. Evidence of hypertension (170/110 mmHg) had been encountered only during her initial examination at that hospital. She had been treated with antibiotics and sedatives for 2 weeks, after which she had been discharged without any medication. Bacteriological examination of the cerebrospinal fluid with direct microscopy and culture had given negative results. Headache had continued, which she described as 'a disturbing feeling of constriction all around the head,' being almost constant in the past 6 months, showing frequent increases in severity to evolve into an attack of throbbing pain localized in the right part of her head and face. These fluctuations had occurred approximately two times a day, lasting for 15 to 20 minutes, ending without any treatment and recurring without a specific trigger. They were accompanied by fatigue, anorexia, vomiting, palpitation, shortness of breath, sweating, trembling, nausea and a feeling of chest discomfort which she described as 'a sense of approaching death'; she also showed aggressive behavior and aimless fidgety limb movements, as ascertained from her mother's account. Between

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attacks, she was described as 'distant, indecisive and sad' by her family; she often complained of being 'tired and bored' and had difficulty in sleeping as well as fits of crying. She was seen by a psychiatrist during one of the sudden increases in headache severity, who noted findings quite similar to those observed during her first attack and gave a diagnosis of panic disorder complicating a major depressive episode; but her family refused to give her any medicine at that time. Attacks were conceived by her family as 'incomprehensible, frightening changes of attitude and behavior which started and ended quite abruptly'; they were convinced that she was simulating an illness to attract their attention. Gradually, nausea increased, appetite decreased, she refused to participate in activities that she liked previously and began to lose weight.

One week before her presentation at our centre, right subcostal pain and intractable vomiting appeared, followed by jaundice. On the initial physical examination, a depressive facial expression and jaundice were observed; a soft, rounded mass was found in the right hypochondrium, which was tender to palpation; blood pressure was normal. Laboratory investigations were notable for total and direct bilirubin levels of 4 and 3.3 mg/dL, respectively, and a fasting venous plasma glucose value of 157 mg/dL; alkaline phosphatase, amylase, alanine and aspartate aminotransferase levels were normal. Her urine was trace positive for ketones. Abdominal ultrasonography revealed a well defined, encapsulated, 8 by 5.8 cm solid mass in the subhepatic area which appeared to arise from the right adrenal gland. Biochemical screening for a hormone-secreting type adrenal tumor revealed increased (14.2 mg; N < 8 mg) 24-hour urinary excretion of vanillylmandelic acid; no evidence of adrenal cortical hyperfunction, thyrotoxicosis or multiple endocrine neoplasia was observed. On the second day of her hospitalization the patient was found wandering in the ward in an agitated and confused state; fever (38.4°C), tachycardia (120 beats/min), hypertension (240/140 mmHg), tachypnea (24/min), flushing, sweating and irritability expressed by violent limb movements and swearing were noted. The suspicion of phaeochromocytoma strengthened with these findings, which disappeared without any intervention in approximately 10 minutes. Prazosin hydrochloride, a selective α-antagonist was given for preoperative preparation. Fluid replacement therapy was given as indicated. During the operation, a large right adrenal mass that did not show evidence of local invasion was found, and right adrenalectomy was performed under a continuous sodium nitroprusside infusion. After adrenalectomy, hypotension appeared but responded promptly to the infusion of dopamine, which was continued for 6 hours postoperatively. Pathological evaluation confirmed the diagnosis of phaeochromocytoma. The patient showed a very good postoperative course; jaundice and all other findings disappeared and she was discharged on the 14th postoperative day without any medication. She has been in an excellent state since her operation and has not experienced any of her previous complaints. The patient and close relatives are being followed-up, since childhood phaeochromocytomas can be bilateral and/or familial.

**DISCUSSION**

Phaeochromocytomas are encountered very rarely in childhood. Samaan et al. reported only two patients under the age of 17 among a total of 41 patients observed at the University of Texas and Tuorn Institute at Houston between 1956 and 1968. Similarly, a recent review of the Queensland population by Hartley and Perry-Kene showed that there had been no patient under the age of 17 over a 14 year period. The experience of the Cincinnati Children’s Medical Center also exemplifies the rarity of this tumor in childhood, since only four patients under the age of 17 were encountered in 20 years.

Phaeochromocytomas can be confused with many unrelated diseases due to their different types of presentation. This extreme variability has led them to earn the reputation of mimics and is most evident in their neuropsychiatric manifestations, some of which are uncommon but bizarre enough to suggest a primary disorder of the central nervous system. On the other hand, atypical presentation of a common symptom like headache can also result in considerable diagnostic difficulty. This can be understood from the acute increases in headache severity observed in our patient, which were notable for their unilateral character and accompanying anorexia, nausea, vomiting and mood disturbances and could have been considered as migraine attacks. Chronic headache of a 'constricting' character was also seen in our case; this could have led to confusion with a tension headache, which has similar properties and is the most frequent form of headache encountered in the population.

The neuropsychiatric aspects of phaeochromocytomas have recently become a subject of interest for many workers, but most observations have been made in adults, possibly because the disease is rare in children. Metzer and Lucy reported a 38-year-old woman with anxiety and depression accompanying phaeochromocytoma. Medvei and Catt described a 37-year-old woman with phaeochromocytoma and acute anxiety attacks during which she became aggressive and paranoid as well as hypertensive; in their accompanying review of the literature for similar case presentations, they noted that psychiatric disturbances, including suicide attempts, had been observed relatively frequently in adult patients with phaeochromocytomas.

Our case report is unique in that it is concerned with a child with phaeochromocytoma and psychiatric findings consisting of depression and panic dis-
order, which were interpreted as being directly related to, since they disappeared after the removal of, the tumor. This observation is in line with prior reports, since all neuropsychiatric changes described in relation with pheochromocytomas, including dementia were found to be reversible. Of particular notice was the fact that depression persisted in the normotensive periods between the attacks of panic and hypertension; this implied that the psychiatric effects of catecholamines continued irrespective of changes in blood pressure. The diagnosis of meningitis given to the patient was probably incorrect since it was not confirmed by bacteriological studies; the findings noted at that time could have resulted from hypertensive encephalopathy. While our patient did not have a convulsive disorder at any stage of her history, Clezy et al. reported a boy presenting with convulsions at a blood pressure level considerably lower than that observed in our patient during an acute attack; this again attests to the variability in the clinical presentation of pheochromocytomas.

Another intriguing aspect of our case was the jaundice that accompanied pheochromocytoma and resolved immediately following its removal. Since no laboratory or intraoperative evidence of an obstructive cause for jaundice was observed, we considered that it could possibly have been due to an adverse effect of catecholamines on hepatic bile excretion, perhaps mediated through deleterious changes in hepatocytes as a result of grossly elevated metabolic activity and of triglyceride accumulation, which are known to accompany states of catecholamine excess. Abdominal pain has been reported frequently in association with pheochromocytomas but jaundice has not been presented previously as a complication of these tumors; we believe that further studies are needed to clarify its pathogenesis.

We conclude that a pheochromocytoma can mimic neuropsychiatric disorders in children as well as in adults and that it should be considered in the differential diagnosis of such disorders, even if hypertension is not present, because hypertension may be quite intermittent (and therefore not detected) while headache and/or psychiatric disturbances may be persistent.

REFERENCES