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Pediatric Articles

ADRENAL HEMORRHAGE IN NEONATES: REPORT OF 5 CASES AND REVIEW OF THE LITERATURE

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ABSTRACT

The differential diagnosis of masses in the suprarenal area in neonates is discussed in relation to clinical, laboratory and radiologic findings. Neonatal adrenal hemorrhage can be accurately diagnosed clinically. In the neonate neuroblastoma in situ is self-limiting and exploration to exclude it is unnecessary. Operative intervention should be reserved for controlling massive adrenal hemorrhage or if an abscess forms.

Adrenal hemorrhage in the newborn is not rare.[1] The first report of massive adrenal hemorrhage diagnosed during life was by Corcoran and Strauss in 1924 and an operation was performed because of intractable bleeding.[2] Many cases have been reported since then, revealing a varied clinical picture and resulting in controversy over the treatment of choice. Some authors recommend surgical evacuation or excision,[3-7] whereas others cite the reliability of clinical and radiological features to justify conservative management.[8-12]

A review of the medical records at this institution between 1965 and 1977 revealed 7 cases of suprarenal hemorrhage in the newborn. Two cases were diagnosed retrospectively by calcification in the region of the adrenals. The 5 cases diagnosed clinically are presented in tables 1 and 2, and the details of case 5 are presented herein.

CASE REPORT

Case 5. A male newborn was referred to us when he was 5 days old. An excretory urogram (IVP), which was done when he was 2 days old because of a left upper abdominal mass, had shown a non-functioning left kidney. Relevant laboratory data included serum bilirubin 10 mg./dl. (decreasing rapidly to 5 mg./dl.), urinary vanillyl mandelic acid 0.3 mg./24 hours, urinary catecholamines 7 μg./24 hours, and hemoglobin 15.7 gm./dl. An IVP when the patient was 6 days old showed a functioning left kidney, with the upper pole displaced laterally by a radiolucent suprarenal mass (fig. 1), which a renal scan with ^{99m}technetium showed to be avascular (fig. 2, *A*). Computerized axial tomography of the abdomen revealed the mass to be cystic, which was confirmed by ultrasonography (fig. 2, *B*). The newborn was treated conservatively. A followup IVP 2 months later revealed the left renal axis to be normal. No mass was palpable then or at 4-month followup. At 9 months an IVP was normal but calcification was absent.

DISCUSSION

The pathogenesis of adrenal hemorrhage of the newborn is not known. Associated factors include birth trauma owing to difficult labor or delivery,[13, 14] asphyxia,[1, 13] septicemia, hemorrhagic disorders[13] and hypoprothrombinemia.[1, 14] The hemorrhage is reported to affect the right adrenal 3 to 4 times more commonly than the left adrenal[1] and it is bilateral in 8 to 10 per cent of the cases. The usual explanation for susceptibility of the right adrenal is its greater likelihood of compression between the liver and spine and, because the right adrenal vein usually drains directly into the inferior vena cava, its proneness to changes in venous pressure.[13]

Of our patients hemorrhage occurred on the right side in 2, the left side in 2 and both sides in 1 (table 1). Birth weights were normal (range 3.49 to 4.63 kg.). No evidence of trauma was present at birth. Four newborns were vertex presentations and 1 had been delivered by cesarean section (indicated by a previous cesarean section). All were born at full term and only 2 had respiratory distress or cyanosis at birth. None had fever, evidence of septicemia, a significant coagulation defect or blood-group incompatibility. In all cases the hemorrhage occurred before 1 week of age (table 1).

Originally, clinical manifestations have been classified as owing to either adrenal insufficiency or acute hemorrhage.[13] Most recent reports indicate that the patient presents with prolonged neonatal jaundice and/or an abdominal mass with a decreasing hemoglobin.[9] Adrenal insufficiency is rare and we could find no proved case in our review of the English literature. In our patients the main clinical features were flank mass in all, prolonged jaundice in 4 and mild anemia in 3 (table 1). All had normal urinary excretion of vanillyl mandelic acid and catecholamines, and none had evidence of adrenal insufficiency.

The radiologic findings have been described repeatedly.[8, 9, 11, 15] The early IVP reveals a smooth, homogeneously radiolucent mass displacing the kidney laterally and inferiorly, and indenting or flattening the superior pole. Non-visualization of the kidney on the side of the adrenal hemorrhage has been reported.[7, 16, 17] In our last 2 cases the early IVP revealed nonfunction of the kidney on the involved side but the next IVP and initial films in the other 3 cases showed the characteristic deviation of the renal axis and lateral displacement of its upper pole by a radiolucent suprarenal mass (fig. 1). The cystic nature of the mass was documented by an operation in case 1 (table 2), arteriography in cases 2 to 4 (fig. 3) and ultrasound, ^{99m}technetium renal scan and computerized tomography in case 5 (fig. 2).

The first patient, who had bilateral hemorrhage, underwent unilateral adrenalectomy and the subsequent 4 patients were managed conservatively (table 2). Shrinkage of the mass was

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TABLE 1. *Relevant history, physical findings and laboratory investigations in the 5 cases of neonatal adrenal hemorrhage*

Case No.	Gestational Age	Birth Weight (kg.)	Delivery and Presentation at Birth	Signs of Respiratory Distress at Birth	Age at Presentation	Presenting Symptoms	Site of Adrenal Hemorrhage	Signs of Adrenal Insufficiency	Coagulation Defect	Direct and Indirect Coombs Test	Hemoglobin (gm./dl.)	Bilirubin (mg./dl.)	Urinary Vanillyl Mandelic Acid and Catecholamines
1	Term	4.16	Normal vaginal (vertex)	No	2 days	Increasing jaundice and bilat. flank masses	Bilat.	No	No	Neg.	11.2	22.2 (direct, 1.24)	Normal
2	Term	4.63	Normal vaginal (vertex)	Yes	4 days	Rt. flank mass	Rt.	No	No	Neg.	17.6, later 14.5	8.5, later 15	Normal
3	Term	3.49	Normal vaginal (vertex)	Yes	Few hrs.	Lt. upper abdominal mass, imperforate hymen, hypertrophy of lt. leg and dislocation of lt. hip	Lt.	No	No	Neg.	15.8	8.9	Normal
4	Term	3.70	Cesarean section (indication previous cesarean section)	No	5 days	Increasing jaundice and rt. abdominal mass	Rt.	No	No	Neg.	15.9, later 13.6	22.5, later 2.1	Normal
5	Term	3.52	Normal vaginal (vertex)	No	2 days	Lt. upper abdominal mass	Lt.	No	No	Neg.	15.7	10, later 5	Normal

TABLE 2. *Radiologic findings and management of 5 cases of neonatal adrenal hemorrhage*

Case No.	Radiologic Findings	Management
1	IVP at age 1 wk.—bilat. suprarenal radiolucent masses displacing the upper poles of both kidneys, IVP at age 2 wks.—rim-like calcification appeared in the radiolucent masses, IVP at age 1 yr.—extensive adrenal calcification developed in the region of the remaining adrenal with return of renal axis to normal	Laparotomy and rt. adrenal removed only
2	Initial IVP—poorly defined mass in the upper pole of the rt. kidney, aortogram—avascular mass, IVP at 1½ mos.—return of the axis of the kidney to normal and the mass much smaller, IVP at 1 yr.—calcification in the rt. adrenal developed	Conservative
3	Initial IVP—deviation of the lt. renal axis, aortogram—an avascular lucent suprarenal mass, IVP at 1½ mos.—the renal axis became normal, at 15 mos.—dense calcification developed	Conservative
4	Initial IVP—the rt. kidney was not visible and the colon was displaced by a mass, aortogram—the mass was avascular, IVP at 2½ mos.—the rt. kidney was visible and in normal position on urography, at 1½ yrs.—dense calcification developed in the rt. adrenal	Conservative
5	Initial IVP at 3 days—non-visualization of the lt. kidney, IVP at age 6 days—lt. suprarenal mass, renal scan—mass appeared avascular, ultrasonography—cystic mass, computerized tomography—cystic density, IVP at 2 mos.—return of the lt. renal axis to normal	Conservative

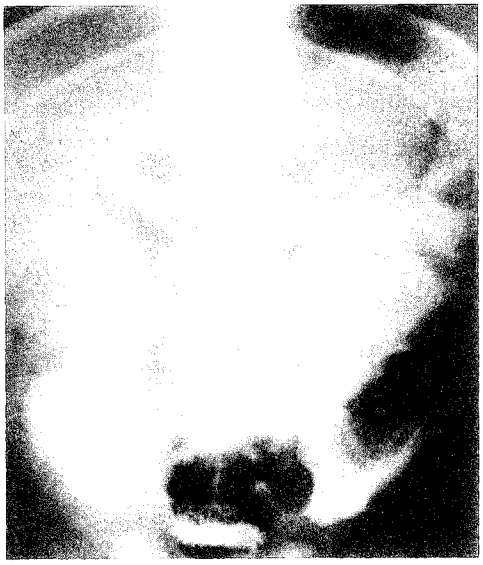

FIG. 1. IVP in case 5 reveals apparently radiolucent left suprarenal mass with lateral renal displacement.

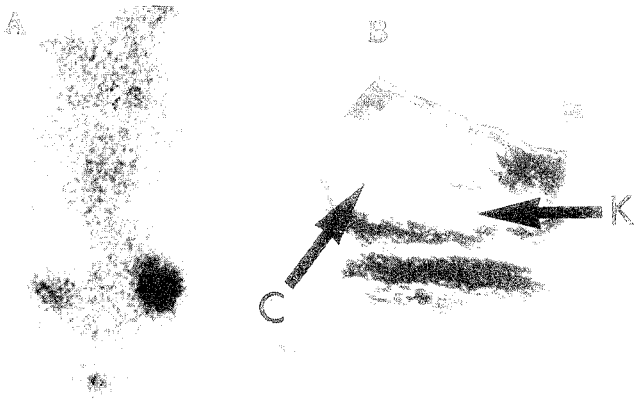

FIG. 2. Case 5. *A*, renal scan reveals avascular mass. *B*, ultrasonography confirms cystic nature of mass. *K*, kidney. *C*, cyst.

apparent clinically at 6 to 8 weeks in all patients. An IVP showed a rim-like calcification in the radiolucent mass at 1 week in case 1 only (fig. 4), return of the renal axis to normal at 6 to 8 weeks in all cases and dense calcification in the region of the hemorrhagic adrenal by 2 years of age in all 4 cases followed for >1 year (fig. 5).

The surgical literature contains few reports of suprarenal hemorrhage in neonates. Some adrenal cysts and pseudocysts may, in fact, have represented previous adrenal hemorrhage. Unfortunately, most of the patients described in the surgical literature underwent laparotomy and in many cases a normal kidney was removed.[7, 16, 18, 19] In 1 case of infected adrenal hemorrhage on the left side the neonate was subjected to en bloc resection of the mass, kidney, spleen and tail of the pancreas in the belief that the mass was malignant.[20] Although infection of the hematoma could occur [13, 17, 20] it was not apparent in our patients.

The differential diagnoses of a flank mass in the suprarenal area in the newborn include adrenal hemorrhage, adrenal cyst,[21] neuroblastoma, Wilms tumor and renal duplication with dilatation of the upper segment. This last condition can be excluded by cystoscopy, or retrograde or percutaneous anterograde pyelography. Cystic masses can be differentiated by IVP, arteriography, ultrasonography, renal scan and/or computerized axial tomography. Thus, Wilms tumor and neuroblastoma can be

excluded readily. There is no adequate explanation for the initial non-visualization of a kidney in a newborn with adrenal hemorrhage, which has been reported by others and occurred in our last 2 cases, but it should not be interpreted as renal invasion by a tumor.

Determination of the 24-hour urinary excretion of vanillyl mandelic acid, homovanillic acid and catecholamines is relevant, since an increase in these substances, particularly vanillyl mandelic acid, is virtually diagnostic of neuroblastoma. In all our patients (in some cases twice) normality of these levels was established before adrenal hemorrhage was diagnosed. Thus, the only remaining entity to be excluded is neuroblastoma in situ or hemorrhage into a neuroblastoma. Farber considers the latter a mechanism of spontaneous remission of this malignant tumor.[22] Sober and Hirsch described a case of neuroblastoma in a hemorrhagic adrenal gland in a neonate, which probably represented neuroblastoma in situ.[18] Other cases of neuroblastoma in situ in neonatal adrenal cysts have been reported.[23]

The significance of neuroblastoma in situ in the newborn is questionable. Beckwith and Perrin, who estimated its incidence in their necropsy material to be about 40 times greater than expected from reported figures for clinically manifest neuroblastoma, postulated that many of these microscopic tumors degenerated or differentiated to normal tissue.[24] This theory gains support from the report by Guin and associates of findings at necropsy of infants <6 months old, who had died of unrelated problems.[25] In patients ≦3 months old the incidence of neuroblastoma in situ was 258 times the frequency expected according to rates for the clinically manifest tumor. In infants 3 to 6 months old, however, they found no such tumors. Therefore, Guin and associates postulated a time-growth relationship in the natural history of neuroblastoma in situ, illustrating the potential for spontaneous resolution.

We conclude that the condition can be diagnosed accurately by history, physical examination, laboratory data and radiographic imaging. An immediate operation to exclude neuroblastoma in situ is not justifiable. By 6 to 8 weeks shrinkage of the mass will be apparent clinically and this, together with straightening of the renal axis, will be visible radiographically. The adrenal will contain calcified deposits by 1 year. Thus, an operation should only be done if the hemorrhage is uncontrollable or to drain the abscess if infection of the hematoma occurs.

This protocol of conservative management applies only for newborns in the first month of life. Thereafter, adrenal hemorrhage may represent necrosis of a malignant tumor or bleed-

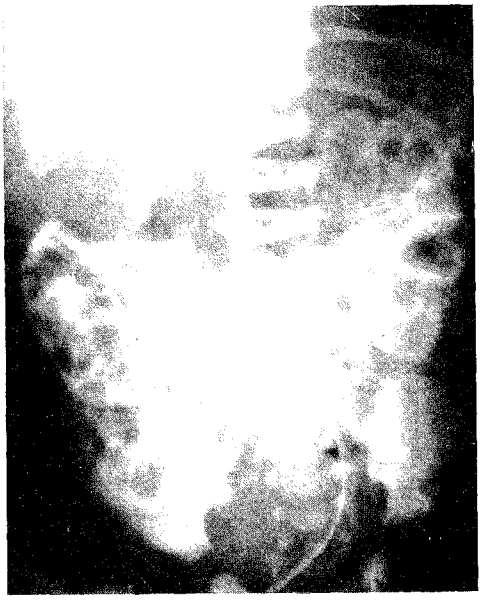

FIG. 3. Umbilical artery arteriography in case 4 shows right mass to be avascular.

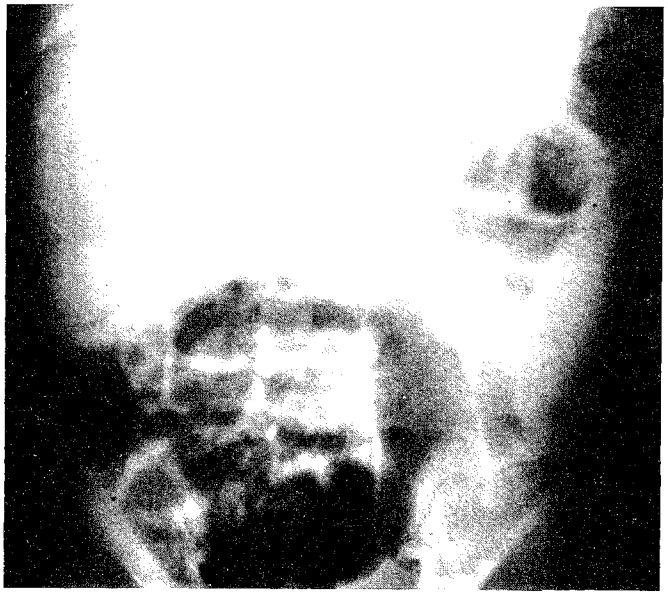

FIG. 4. Note rim-like calcification in bilateral radiolucent masses in case 1 when patient was 2 weeks old.

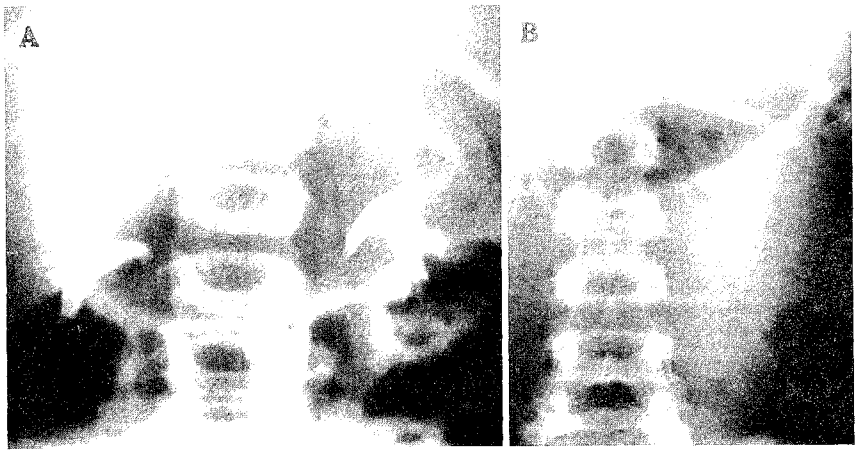

FIG. 5. *A*, IVP in case 2 when patient was 1 year old shows normal right renal axis. *B*, flat plate of abdomen in case 1 reveals dense calcification in region of left adrenal.

ing into it, warranting surgical exploration. Craig and associates reported adrenocortical carcinoma in a 10-month-old child in whom the radiological findings were similar to those of an adrenal hematoma.[26]

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EDITORIAL COMMENT

The diagnosis of idiopathic adrenal hemorrhage in the newborn is suspected when a mass, jaundice and anemia are associated with inferior dislocation of the kidney on an IVP or renal scan. Ultrasonography, often showing a mixed lucent pattern, is confirmatory.

We have seen 2 patients with simultaneous idiopathic adrenal hemorrhage and renal vein thrombosis. One had ipsilateral and the other contralateral involvement, with non-visualization of the involved kidney on the IVP. This may be the explanation for the non-visualization in 2 patients presented. The presence of hematuria would lead one to suspect renal vein thrombosis and a decreased platelet count or other evidence of consumptive coagulopathy strongly supports this presumption. The treatment remains the same—that is fluid support—without the necessity for surgical intervention.

These authors review another example of the role of multi-modality evaluation in the child with an abdominal mass. Exploratory surgery becomes less and less common as we learn to base our diagnostic studies in an organized manner, using the tools available to our radiologic associates. With knowledge of the natural history of various problems and an accurate diagnosis patients can be managed non-operatively with confidence. Does multicystic renal disease (cystic dysplasia) fall into a similar category?

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