CASE REPORT

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Acute Cerebellar Hemorrhage in a Patient with Klinefelter Syndrome: XXY Karyotype Obtained Postmortem from Cells from Pericardial Fluid

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ABSTRACT: A case of Klinefelter syndrome and a spontaneous cerebellar hemorrhage in a 12-year-old boy is presented. Autopsy revealed that the hemorrhage was due to the rupture of a dilated artery in an arteriovenous malformation in the right cerebellar hemisphere. The small, undescended testes exhibited partial atrophy of the seminiferous tubules. Postmortem chromosome analysis of cells from the pericardial fluid demonstrated a 47, XXY karyotype. He had previous surgical treatment for bilateral thumb polydactyly and patent ductus arteriosus. In juvenile cases of sudden death with overlapping morphological dysgenesis, postmortem karyotyping may provide important diagnostic information.

KEYWORDS: forensic science, Klinefelter syndrome, postmortem karyotyping, cerebellar hemorrhage, polydactyly, patent ductus arteriosus

Spontaneous cerebellar hemorrhage accounts for 10% of all cases of intraparenchymal central nervous system hemorrhage, and arterial hypertension is the commonest (50–70%) predisposing factor, occurring most often in the 6th, 7th, and 8th decades of life (1–4). However, pediatric cerebellar hemorrhage is much less common and is usually associated with arteriovenous malformation, tumors in the posterior fossa, blood dyscrasias, and trauma (5). This is a case report of fatal cerebellar hemorrhage in a preadolescent male with karyotype 47, XXY Klinefelter syndrome. The karyotype was obtained by postmortem analysis of cells obtained from pericardial fluid.

Case Report

A 12-year-old Japanese boy was found dead in his bed in the morning. The day before, he had complained of a headache while playing soccer with his friends after school and that evening, had gone to bed without eating dinner. Thirty minutes later, his mother had noticed that he was febrile and was sweating in his sleep.

He was born after 40 weeks of gestation, with an uneventful delivery, but with moderate intrauterine growth retardation, and a birth weight of 2380 g. He was treated surgically for bilateral thumb polydactyly at one year of age and for repair of a patent ductus arteriosus (PDA) at two years old.

Postmortem Chromosome Analysis

The autopsy was started in the afternoon of the same day, at which time the rectal temperature was 29°C, and the postmortem interval was estimated to be 12–16 h, using a nomogram based on the relationship between rectal temperature and time of death (6). During the postmortem examination, samples of pericardial fluid and blood were obtained and immediately sent to SRL Inc. (Tokyo, Japan) in a sterile container in transportation medium for cytogenetic analysis. As the blood sample was substantially hemolyzed, viable cells were not harvested for karyotyping. Standard trypsin G-banding analysis was performed during the metaphase on cells obtained from phytohemagglutinin-stimulated lymphocytes from pericardial effusion, according to standard procedures. The karyotype of the deceased was determined to be 47, XXY from 13 metaphase preparations of pericardial cells.

Autopsy Findings

At autopsy, the body measured 143.5 cm and weighed 29 kg. A recent 3.8 cm hematoma occupied the right cerebellar hemisphere, tightly compressing the medulla oblongata (Fig. 1*a*). In the right cerebellar parenchyma adjacent to the hemorrhage, there was an arteriovenous malformation (Fig. 1*b*), and rupture of a dilated artery was observed (Fig. 1*c*).

Other findings were related to hypogonadism. The penis was hypoplastic (Fig. 2*a*), and the testes, small and firm, were present in the inguinal canals (Fig. 2*b*). Histologically, approximately two-thirds of the seminiferous tubules were normally developed, the remainder being atrophic, with thick hyalinized basement membranes. Anomalous proliferation of the rete testis was observed (Fig. 2*c*). The clinical history and gonadal abnormalities prompted us to perform the chromosomal analysis, described above, that revealed the karyotype of the deceased to be 47, XXY (Fig. 2*d*).

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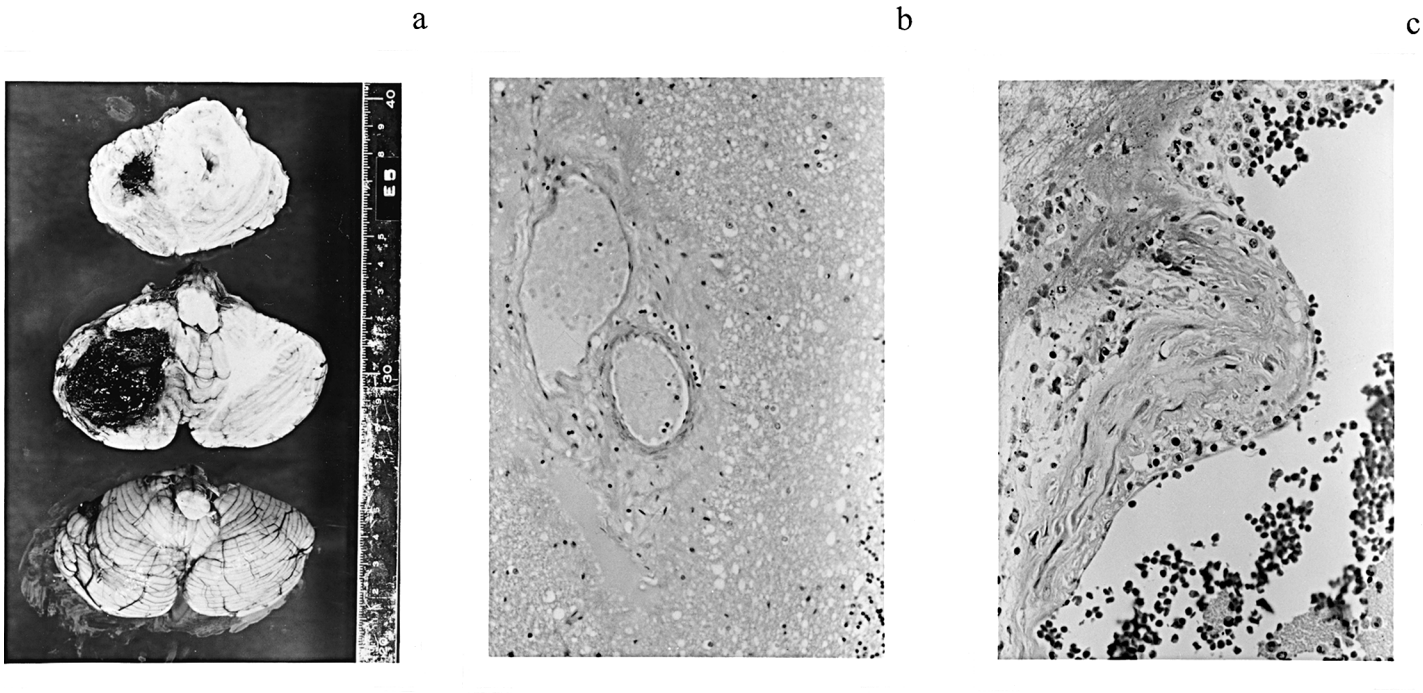

Figure 1

FIG. 1—*Intracerebellar hemorrhage.* a. *Hematoma (length 3.8 cm, width 3.2 cm, depth 2.5 cm) of the right cerebellar hemisphere.* b. *Arteriovenous malformation of the right cerebellar hemisphere, in which a dilated anomalous artery can be observed accompanying the vein (hematoxylin-eosin staining, ×25).* c. *Rupture of the dilated artery demonstrated by serial section of the hematoma (hematoxylin-eosin staining, ×100).*

In addition to the clinical features of Klinefelter syndrome, there were surgical scars consistent with the clinical history of polydactyly and PDA.

The cause of death was acute hemorrhage of the right cerebellar hemisphere.

Discussion

Spontaneous intracerebellar hemorrhage carries a high mortality, which frequently results in sudden death (1). In the present case, the deceased was a 12-year-old boy in whom the hemorrhage occurred in the right cerebellar hemisphere. Microscopic examination of the hematoma revealed that the hemorrhage was caused by the rupture of a dilated artery in an arteriovenous malformation.

In addition, the deceased exhibited the somatic characteristics of Klinefelter syndrome previously described and a 47, XXY karyotype. Klinefelter syndrome has been reported to be associated with a wide variety of disorders including cancers of breast and extra gonadal germ cells, autoimmune disorders, intellectual and psychiatric disorders, osteoporosis, and vascular abnormalities (7). Fricke et al. (8) pointed out that mitral valve prolapse was a frequent finding in Klinefelter syndrome. Said et al. (9) reported a case of coronary-cameral fistula in association with Klinefelter syndrome. Subarachnoid hemorrhage has been reported in patients with Klinefelter syndrome (10–12).

In the present study, we present a case of Klinefelter syndrome associated with the rupture of an arteriovenous malformation causing fatal hemorrhage in the right cerebellar hemisphere, patent ductus arteriosus and polydactyly. In a similar case, Woods et al. (13) reported "disorganization syndrome" in a male infant with a partial foot arising from the right buttock, a shortened right leg with severe non-positional talipes equinovarus, unilateral narrowing of the common iliac artery, and absence of the right kidney, whose karyotype was 47, XXY. We have found that postmortem chromosome karyotyping provides useful information for diagnostic and genetic counseling purposes in pediatric forensic cases with overlapping malformations.

Postmortem karyotyping is most productive when multiple malformations are found in a perinatal autopsy (14). For example, cytogenetic examination was utilized to demonstrate an association of fetal congenital heart malformations with chromosome anomalies in abortions and stillbirths (15). Karyotyping is performed using various fetal tissues, including skin, placenta, proximal limb muscle, and cardiac blood. However, the success rate of karyotyping is uniformly low in stillbirths (16,17). Kyle et al. (18) reported that the failure rate of postmortem karyotyping after termination of pregnancy for congenital abnormalities was 27%, and that the main reasons for failure to obtain a positive result were "no growth" or an infected sample. The high failure rate was significantly influenced by the time interval between termination of pregnancy and sampling. The median interval in unsuccessful culture was 4 days (range 2–13 days), whereas that in successful karyotyping was 3 days (range 1–7 days). In our case, the postmortem interval, which was estimated to be 12–16 h, was found not to have impeded chromosome analysis of pericardial cells. Since the blood sample was substantially hemolyzed, resulting in failure of postmortem karyotyping, the use of cadaveric blood may not be practical for karyotyping in cases with this postmortem interval.

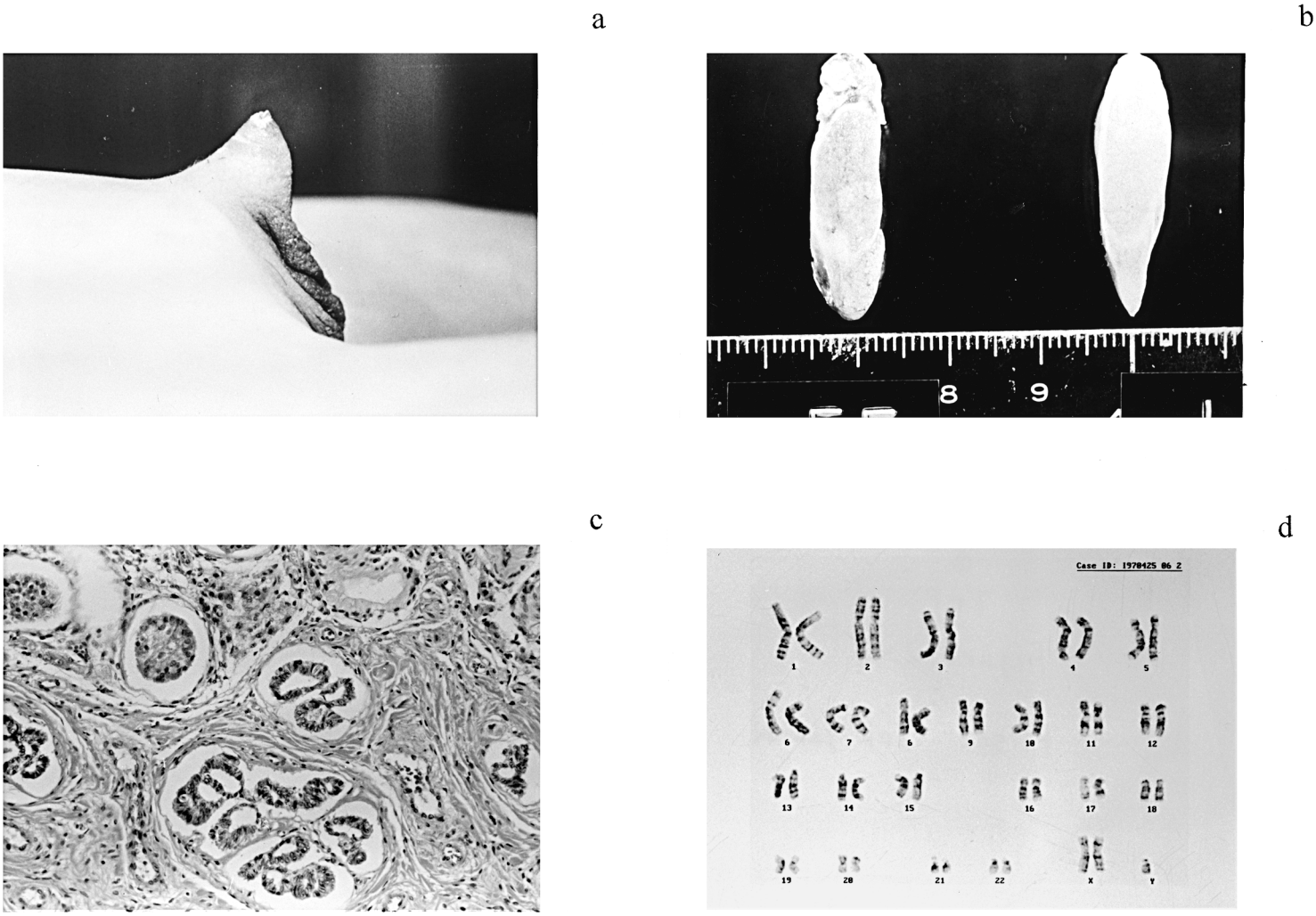

Figure 2

FIG. 2—*Associated features of hypogonadism.* a. *Hypoplastic penis.* b. *Testicular dysgenesis. The testes measured 1.6 cm × 0.8 cm.* c. *Histological view of the testis, demonstrating atrophy of the seminiferous tubules (hematoxylin-eosin staining, ×50).* d. *Postmortem chromosome analysis of the karyotype 47, XXY of the deceased.*

References

1. Fisher CM, Picard EH, Polak A, Dalal P, Ojemann RG. Acute hypertensive cerebellar hemorrhage: diagnosis and surgical treatment. J Nerv Ment Dis 1965;140:38–57.
2. Abud-Ortega AF, Rajput A, Rozdilsky B. Observations in five cases of spontaneous cerebellar hemorrhage. CMAJ 1972;106:40–2.
3. Freeman RE, Onofrio BM, Okazaki H, Dinapoli RP. Spontaneous intracerebellar hemorrhage, diagnosis and surgical treatment. Neurology 1973;23:84–90.
4. Vincent FM. Cerebellar hemorrhage. Minn Med 1976;59(7):453–8.
5. Chadduck WM, Duong DH, Kast JM, Donahue DJ. Pediatric cerebellar hemorrhages. Child's Nerv Syst 1995;11:579–83.
6. Henssge C. Death time estimation in case work. I. The rectal temperature time of death nomogram. Forensic Sci Int 1988;38:209–36.
7. Smyth CM, Bremner WJ. Klinefelter syndrome. Arch Intern Med 1998;158:1309–14.
8. Fricke GR, Mattern HJ, Schweikert HU. Mitral valve prolapse in Klinefelter syndrome. Lancet 1981;8260–61:1414.
9. Said SAM, Bucx JJJ, van de Weel FA. Coronary-cameral fistula in association with Klinefelter syndrome: exercise-induced ventricular tachycardia late after surgical ligation. Int J Cardiol 1992;36:111–4.
10. Lundberg PO. Sex chromosome and cerebrovascular abnormalities. Lancet 1966;7478:1422.
11. Price WH, Steers AJW, Wilson J. Subarachnoid hemorrhage and Klinefelter syndrome. Lancet 1982;8294:380.
12. Monk B. Vascular abnormality in Klinefelter's syndrome? Lancet 1982;8296:491.
13. Woods CG, Treleaven S, Betheras FR, Sheffield LJ. Disorganization-like syndrome with 47,XXY and unilateral narrowing of the common iliac artery. Clin Dysmorphol 1995;4:82–6.
14. Chambers HM. The perinatal autopsy: a contemporary approach. Pathology 1992;24:45–55.
15. Tennstedt C, Chaoui R, Korner H, Dietel M. Spectrum of congenital heart defects and extracardiac malformations associated with chromosomal abnormalities: results of a seven year necropsy study. Heart 1999;82:34–9.
16. Bauld R, Sutherland GR, Bain D. Chromosome studies in investigation of stillbirths and neonatal deaths. Arch Dis Child 1974;49:782–8.
17. Smith A, Bannatyne P, Russel P, Ellwood D, den Dulk G. Cytogenetic studies in perinatal death. Aust NZJ Obstet Gynaecol 1990;30:206–10.
18. Kyle PAM, Sepulveda MW, Blunt S, Davies G, Cox PM, Fisk NM. High failure rate of postmortem karyotyping after termination for fetal abnormality. Obstet Gynecol 1996;88:859–62.

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