DYSKINETIC CILIA SYNDROME ASSOCIATED WITH POLYCYSTIC KIDNEY DISEASE AND PRIMARY INFERTILITY

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SUMMARY

The Dyskinetic Cilia Syndrome is believed to be an inherited disorder characterized by flagellar and ciliary defects. In spermatozoa the defect results in immotility, subsequent inability to penetrate cervical mucous and infertility.

A case is reported of a male with polycystic kidneys and ultrastructural evidence of axonemal defects in the spermatozoa associated with infertility.

Introduction

The aetiology of infertility can be attributed partly or wholly to the "male factor" in 50 per cent of the cases. Diminished fertilizing potential is often related to oligoasthenospermia. The aetiology of asthenospermia in morphological ly normal appearing sperm is not always known. The two likely causes are a genetic anatomic structural abnormality or a post-translational enzyme disorder. A rare disorder in which sperm immotility results from a structural defect in the axoneme is reported.

CASE REPORT

A 32 years old White male presented for evaluation and treatment of primary infertility of five years duration. His medical history was significant for Polycystic Kidney Disease. He had minimal changes in renal function. He also had hypertension which was controlled with Hydrochlorthiazide and Propanolol. He gave a history of recurrent episodes of respiratory tract infection. X-ray chest showed an 8 mm granuloma in the right upper lung field. His mother also had Polycystic Kidney Disease and Hypertension. Physical examination was essentially negative. He had a normal male phenotype. Testicular size and location were appropriate. Serum Testosterone, F.S.H., L.H. and Prolactin levels were within normal limits.

Several semen analyses were done during the course of his infertility workup. Counts ranged from 10 to 30 mill/ml and motility from 0 to 10%. Volume of semen was normal (1 to 2 ml). Sperm morphology was within normal limits.

After several unsuccessful attempts at artificial insemination with husband and donor, the patient was referred to us for possible enrollment in our in vitro fertilization programme. Transmission electron microscopy of spermatozoa revealed significant defects in the sperm axoneme. Numerical aberrations were present in the 9 plus 2 organization of the microtubular pattern that is characteristic of all eukaryotic organisms. Deletion of peripheral doublets, absence of central singlets (9+0 defect), transposition of a single microtubule in the periphery and absence of some of the outer dense fibers were noted in several axonemes. (See

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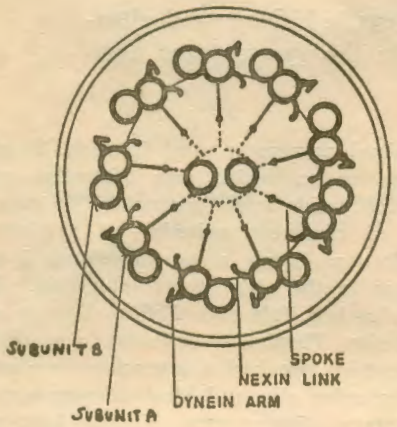
Figs. 1, 2 and compare with 3 and 4 which demonstrates the normal appearance of the axoneme.) Ultrastructural examination of nasal cilia was not performed.

Since previous attempts at intrauterine insemination with husband and donor were unsuccessful, the couple was given the option of either micromanipulation and microinjection of husband s spermatozoa or using donor sperm for in vitro fertilization. They opted for using donor sperm as they were concerned about the possibility of transmission of Polycystic Disease to the offspring. In vitro fertilization with donor sperm resulted in a singleton pregnancy which is currently ongoing.

FIGURE IV



CROSS-SECTION OF THE AXONEME.

Discussion

The integrity of the sperm flagellum is important as the spermatozoan has to pass many obstacles before it can penetrate the egg investments. The intact axoneme consists of a system of microtubules extending from the connecting piece to the tip of the flagellum. The system consists of nine double peripheral microtubules arranged in a circular fashion around two central single microtubules. Each peripheral microtubule has a complete Subunit A and an incomplete Subunit B which is attached to Subunit A. The latter has two arms made up of dynein. Nexin links connect Subunits A and B. Radial spokes from Subunit A attach to the helical sheath surrounding the central microtubules. The undulating motion of beating flagella and the oscillating motion of cilia are induced by the sliding movement of the microtubules (Azfelius, 1959). The microtubules are surrounded for the most of their length by a system of nine outer dense fibers. These impart elastic rigidity to the flagellum and assist in its motility. They also protect the axonemal elements from damage during the sperm's journey through the female reproductive tract.

The Dyskinetic Cilia syndrome (Rossman, 1981) describes a condition in which there may be an absence of dyein arms or the presence of defective radial spokes or there may be microtubular translocation. Three major types conform to this syndrome. Type I shows defective dynein arms. Type II has defective radial spokes and Type III exhibits microtubular translocation. Ciliary epithelia in the nasal cavity, paranasal sinuses, respiratory tract, middle ear, oviducts, cornea, embroyonic tissues and sperm tails may be affected although there are cases in which the cilia are affected but not the spermatozoal tails (Herzon, 1980; Jonsson, 1982).

The other manifestations of the Dyskinetic Cilia Syndrome are reduced or absent mucociliary clearance, bronchiactesis, chronic ear and sino-pulmonary infections and situs viscerum inversus.

Sperm defective in the outer dense fibers display sliding motility (Feneux, 1985).

Our patients had polycystic kidneys with Dyskinetic Cilia Syndrome but no situs viscerum inversus. There is one previous report of the association of these three defects in a single individual (Saeki, 1984).

Although extracorporeal fertilization and assisted fertilization techniques like zona drilling and sperm micromanipulation can help in this form of infertility, concern regarding the genetic transmission of undesirable defects has been expressed.

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See Figs. on Art paper I