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Retinoblastoma tells the story of our health care system

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Retinoblastoma tells the Story of our Health Care System

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Abstract

Objective: To review cases of retinoblastoma.
Setting: Department of Pathology Aga Khan University Hospital Karachi.
Method: Twenty three specimens from cases of retinoblastoma received over a period of eight years were routinely processes and stained with haematoxylin and Eosin stain Other stains were used for tuberculose and melanin. Immunochemistry was resorted to in undifferentiated tumors.
Results: Over 60% cases of retinoblastoma were diagnosed after 5 years and nine cases showed involvement of opti-nerve.
Conclusion: Late diagnosis of retinoblastoma effects the stage of the tumors and the prognisis (JPMA 50:410, 2000).

Introduction

Retinoblastoma is the second most common primary intra-ocular neoplasm in any age group[1]. In childhood this is the third commonest tumor alter leukemia and brain tumors. This is a rare tumor, which arises from the developing retina. From point of cancer biology, tumor is very important as the first human tumor suppresser gene, (lie retinoblastoma susceptibility gene (RB 1) was first demonstrated in this tumor [2,3]. Genetic studies of retinoblastoma have yielded unique insights into familial cancer syndromes and the mechanisms of oncogenesis by tumor suppressor genes. Tumor is worldwide in its distribution, effecting alt races.
Prevalence of retinoblastoma has been examined in a number of populations worldwide and occurs approximately once in even 15000 live births[2]. Population based studies are unfortunately non-existent in Pakistan, therefore, prevalence of this tumor is unknown here. We have reviewed the cases of Retinoblastoma received in the Department of Pathology. The Aga Khan University between the years 1991-1998, with a view to have preliminary information about this tumor.

Material and Methods

During this eight-year period we received 126 biopsies from eye lesions along with 7 fluids for cytologic examination; out of which 23 cases were reported as retinoblastoma. The specimen were routinely processed as these were received fixed in 10% formalin. After processing 5mm sections were cut and stained with Hematoxylin arid Eosin stain. Special stains such as periodic acid Schiff for Fungus, Ziehl Neelson stain for tuberculosis and Masson Fontana for melanin were used where required. Immunohistochemistry (peroxidase anti-peroxidase technique) was resorted to in case of undifferentiated tumors. Markers used include cytokeratin CAM5.2 and AE1/AE3, LCA, L26, UCHL. Vimentin, Desmin. Neuron specific enolase, neurofilanient and GFAP.

Result

A total of twenty-three retinoblastoma cases were diagnosed during this period (Table). Histologic feature typically seen in these cases was tumor formed by small round cell showing differentiation towards retinal structure i.e., formation of Flexner Wintersteiner rosettes,

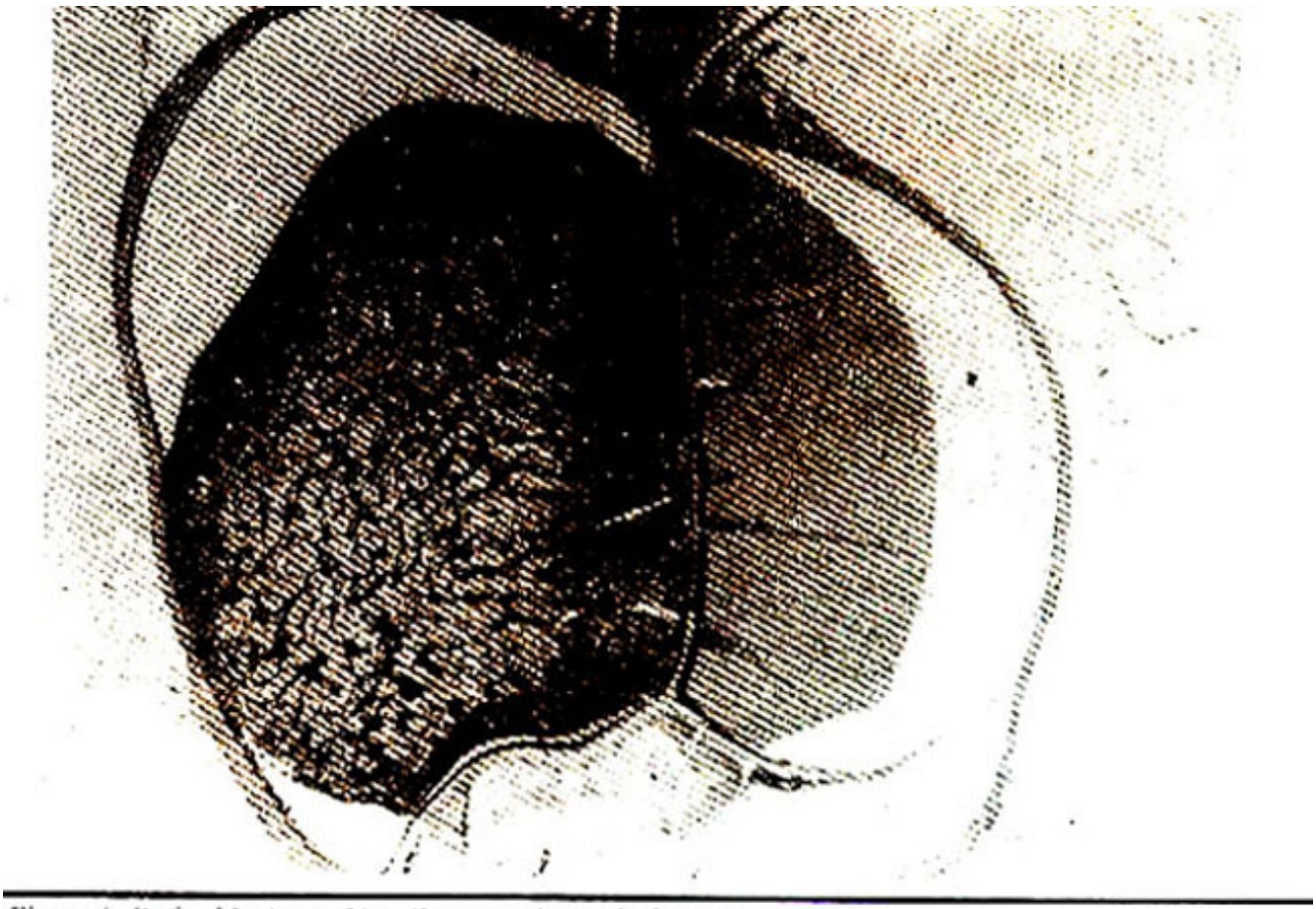

Figure 1. Retinoblastoma: Usually grows inwards from neural retina and fills vitreous compartment of eye

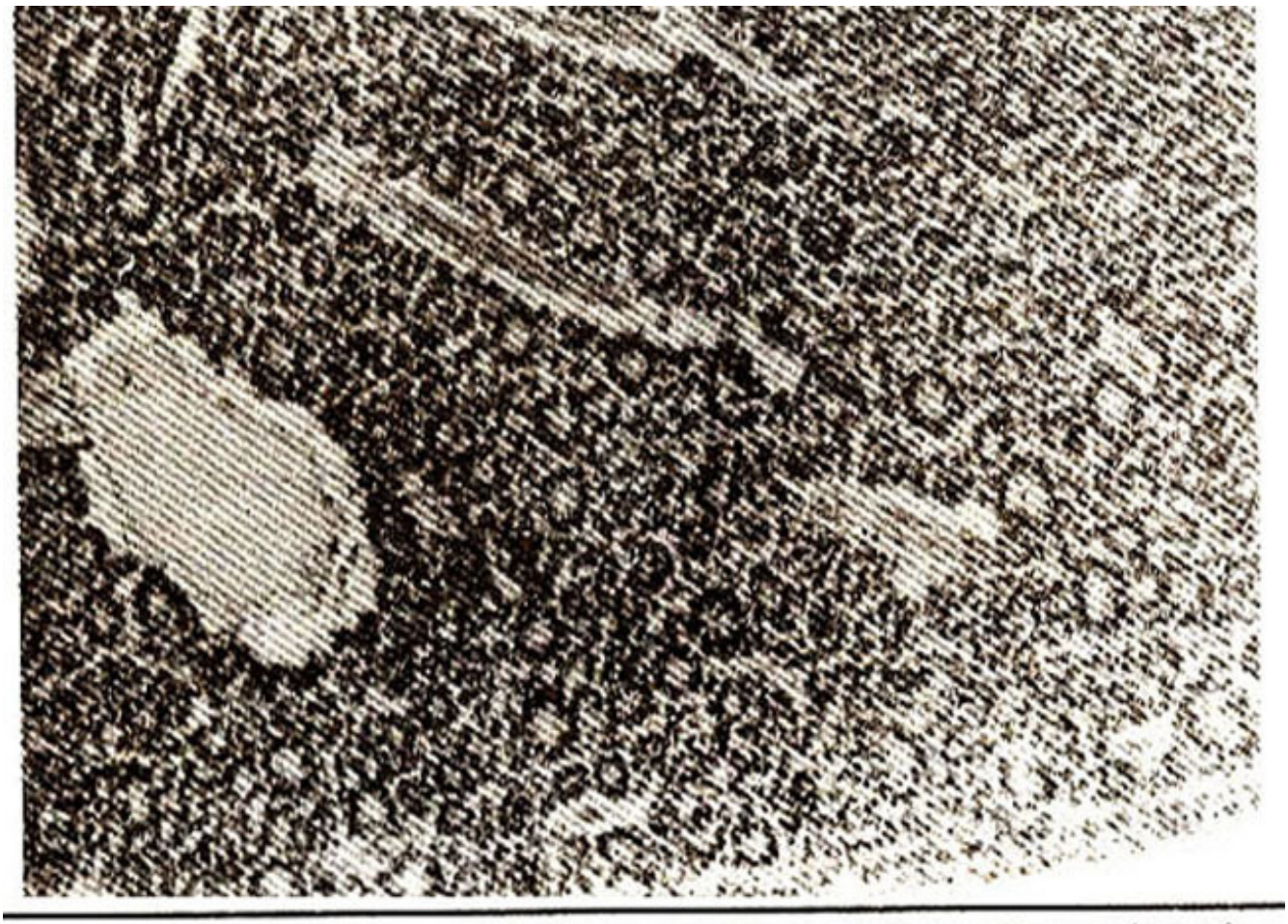

Figure 2. Retinoblastoma: Tumor cells are characteristically arranged to form Flexner-Wintersteiner rosettes.

Figures 1 and 2 and Homer Wright rosettes[4]. None of these cases fell into benign category of retinocytoma which shows numerous Fleurettes, lack necrosis or mitotic activity. The mean age at diagnosis was 5 years, 5 months. Over 60% cases were diagnosed alter 5 years. Nine out of 23 eases showed involvement of the cut end of optic nerve. Twelve cases were seen in males and ten in females. Gender information was not available in one case.

Discussion

Over last one decade significant improvement in understanding of the histogenesis, diagnosis and prognosis of retinoblastona has developed. Tumor arises from developing retina and occurs in unilateral, bilateral and trilateral (Bilateral retinoblastoma plus pineal tumor equates trilateral retinoblastoina) forms[5]. The genetic susceptibility to retinoblastoma is transmitted as an autosomal dominant trait. Most bilateral retinoblastonia carry a germ line predisposition to retinoblastoma. Cytogenetically there is karvotypic deletion on the long arm of human chromosome 13 (13q14). The human retinoblastoma susceptibility gene, RB I has been isolated[3]. The RB 1 protein during cell growth undergoes phosphorvlation in a cell cycle dependant fashion. This interacts with a number of viral oncoproteins. Patients who survive bilateral retinoblastoma have a high lifetime risk of developing a number of other tumors particularly osteosarcoma [6]. Somatic mutation in RB 1 gene are important in a number of tumors which include osteosareoma. breast carcinoma, small cell carcinoma of lung, leukemia, glioblastoma etc[7] Loss of RB 1 gene is associated with worse prognosis in these tumors. lmmunohistochemically retinoblastorna cells have shown positivity for neuron specific enolase (NSE)

and glial fibrillary acidic protein (OFAP) suggesting capacity of primitive stein cells to differentiate in both neuronal and neuroglial direction[8]. Prognostic factors of importance in retinoblastoma are degree of differentiation, choroidal or scleral invasion and most importantly optic nerve extension. The mortality rate associated with optic nerve invasion upto the lamina cribrosa is 15 percent, beyond the lamine cribrosa, 44 percent and to the line of resection 65 percent[9].

There is significant variation in the age at diagnosis, distribution of disease stage and hence mortality of retinoblastoma in different parts of the world. In United States average age diagnosis is 13 months whereas in our data it is 5.5 years. Eighty nine percent of these cases are diagnosed before 3 years of age in USA, in Pakislan 60% of cases are diagnosed after 5 years. The late diagnosis significantly effects the stage of the disease and hence prognosis. In our data 9 out of 23 cases showed involvement of the cut end of optic nerve which is associated with 65-67%, five years metastatic risk.

Diagnosis at an early age in the United States and West could explain the high incidence of low stage disease in infants. The differences in the diagnosis reflect different paediatric health care systems in different countries. Recently a study looked into differences in the pattern of neuroblastoma - another pediatric tumor in four European countries i.e., France, Austria, Germany and UK[10]. ln United Kingdom, the diagnosis is delayed because of less rigorous system of health checks for children, In Germany and Austria each child undergoes nine health checks before the age of 5 years. With 6 health checks in the first year of life. Compliance rates are very high (90-95% up to age of 2 years). Financial support to parents is conditional to attendance of these health checks. France has a structured pediatric health care system in which children are offered a free examination each month for first year of life and financial support is dependent on 3 attendances over first two years. In United Kingdom only five health checks are scheduled during the first 5 years of a child's life and there are no financial incentives for attendance.

Where do we stand in Pakistan as far as pediatric or adult health care system is concerned? Is there any system, which we can quote here for comparison to these countries? In my guess, more than ninety percent of our population is at the mercy of nature. Most of this population is uneducated without any health awareness. No screening program exists for any disease let alone retinoblastoma. This calls for urgent measures to invest in health and education of the nation with substantial emphasis on training of manpower, provision of equipment and methods to cure diseases, Greater expert health surveillance programs are needed for infants and adults with prevention and early diagnosis at the back of the mind.

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