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Neoplasms of the Sella Turcica Region in Ibadan, Nigeria

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Summary. Thirty-two cases of neoplasms of the pituitary gland encountered in Africans at the University College Hospital in Ibadan include twenty-two adenomas and ten craniopharyngiomas, the latter present almost exclusively in the male in the first decade of life. Disturbances of vision and headaches were prominent. The age peaks for both neoplasms were a decade younger in this African group. About one-third of the adenoma patients showed acromegalic features. Details of the clinical picture and neuroradiologic characteristics of each neoplasm at Ibadan have been reviewed.

In their cytologic and tissue cultural behaviour by phase microscopy in this series chromophobe adenoma cells survived more rapidly than the eosinophilic tumour cells in tissue culture. The adenomas form 11·9% and the craniopharyngiomas 5·96% of the 134 various intracranial masses recorded at Ibadan. These ratio frequencies are decidedly higher than the larger Western series have shown.

Résumé. 32 cas de néoplasmes de la glande pituitaire chez des Africains à l'University College Hospital d'Ibadan comprennent 22 adénomes et 10 crâniopharyngiomes, ces derniers presqu'exclusivement chez des enfants mâles de moins de 10 ans. Des troubles de la vision et des céphalalgies etaient fréquents. La pointe d'âge pour les deux néoplasmes était de 10 ans plus basse dans ce groupe d'Africains. Environ un tiers des malades atteints d'adénome presentaient de l'acromegalie. Les details du tableau clinique et les caractéristiques neuroradiologiques de chaque néoplasme sont exposés.

Dans leur comportement cytologique et culturel tissulaire sous microscopie à phase contrastée dans cette série, les cellules chromophobes d'adénome ont survécu plus rapidement que les cellules de tumeurs éosinophiles en culture tissulaire. Les adénomes constituent 11,92% et les craniopharyngiomes 5,96% des 134 masses intracrâniennes diverses enregistrées à Ibadan. Ces rapports de fréquences sont nettement plus élevés que ceux des séries occidentales plus grandes.

INTRODUCTION

Among the thirty-two primary intracranial tumours presented by Billinghurst (1966) in the Ugandan Africans were three craniopharyngiomas and two pituitary adenomas. These

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five neoplasms form 8·77% of all the fifty-seven intracranial neoplasms (ICN) found at the Mulago Hospital in Kampala from 1953 to 65. In their forty-three cases of intracranial masses (ICM) Collomb *et al.* (1963) had only three of these two types of neoplasm, a frequency of 7% ICM. Of the 213 cases of CNS primary tumours in the Bantu Africans reported by Froman & Lipschitz (1970), thirteen (6.103% ICN) were pituitary tumours and seven (3.03% ICN) were shown to be craniopharyngiomas; a total frequency of 9.133% ICN for these neoplasms. At Ibadan of the forty-six cases of intracranial tumours previously reported by Odeku & Janota (1967), three (6.5% ICM) each were craniopharyngiomas and pituitary adenomas (combined frequency of 13% ICM) which is higher than any of the other short African series. This paper presents the details of thirty-two neoplasms of the region of the sella turcica encountered at the University College Hospital in Ibadan, Nigeria, mostly in a 9-year period from 1963 to 71 when thirty of them were recorded. In 1960–61 two neoplasms derived from the pitutary gland had been seen.

ANALYSIS OF THIRTY-TWO NEOPLASMS OF THE SELLA TURCICA REGION

This series of neoplasms consists of twenty-two cases of adenomas of the anterior lobe of the pituitary gland and ten of craniopharyngiomas (craniostomatomas) probably from squamous cell nests along the pars tuberalis of the gland developmentally misplaced or brought about by metaplasia of the chromophobe cells and transitional B-cells (Hunter, 1955; Russell & Rubinstein, 1963). Thus, of the total of 134 intracranial masses reviewed in Ibadan by Odeku *et al.* (1970), the pituitary adenomas constitute 11·9% ICM and the craniopharyngiomas 5·96% ICM (i.e. total of 17·88% ICM for both tumours), and 13·67% ICN and 6·84% ICN of the 117 neoplasms respectively. In a more recent analysis of 186 brain tumours in Ibadan (Odeku *et al.*, 1972) the pituitary adenomas and craniopharyngiomas form 13·01% ICN and 5·90% ICN respectively of the 169 neoplasms and together make up 17·20% ICM of the 186 tumours. No primary neoplasm of the posterior lobe (pars nervosa) of the pituitary gland has been seen in our clinic. Thirteen of the patients with pituitary adenoma were Yorubas, five were Ibos and two were Hausas and one each Fulani and Efik. In the craniopharyngioma group, four each were Yorubas and Hausas and two were Ibos.

Age and sex distribution

In the pituitary adenoma group there were ten males and twelve females; nine being in the fourth decade of life, six in the third, five in the fifth and only two in the sixth. The oldest patient was a 56-year-old man. Of the ten patients with craniopharyngiomas, nine were males. Seven were in their first (peak) decade, two in the second and one in the third decade. The youngest patient was a 3-year-old boy.

General clinical picture

The symptomatology presented by patients with neoplasms are clearly shown in Table 1. Except for vomiting, which is not prominent, the symptom complex in the craniopharyngioma group is similar to that in the series of Matson & Crigler (1969). With each type of neoplasm, headaches and impaired vision are the two most pressing complaints. The classical bitemporal visual defect was well established in a number of the patients. In addition to the signs and symptoms listed in Table 1, one patient each had confusion and associated

menorrhagia in the pituitary adenoma group and mental retardation, epistaxis and ataxia in the craniopharyngioma group. The diabetes insipidus observed was usually transient, but was problematic only in the cases of craniopharyngioma in which two patients required pitressin tannate therapy. Retardation of growth (or small stature) was not a striking feature in the craniopharyngioma group. The duration of symptoms was shorter than 1 year in four and in seven and between 1 and 5 years in fifteen and three in the adenoma and craniopharyngioma groups respectively at the time the patients first came to the hospital. In three patients with adenomas the duration of illness had been quite prolonged—7–12 years.

TABLE 1. Symptomatology on presentation at hospital

	No. of patients		
Pituitary adenoma		Craniopharyngioma	
Impaired vision (six with blindness)	19	Headaches	7
Headaches	18	Impaired vision (one with blindness three with papilloedema)	6
Somnolence/coma	5	Diabetes insipidus	5
Acromegaly	6	Somnolence/coma	3
Amenorrhoea	5	Hemiparesis	4
Weight gain	5	Convulsion	2
Libido loss, impotence	4	Personality changes	2
Hemiparesis	2	Infantilism	1

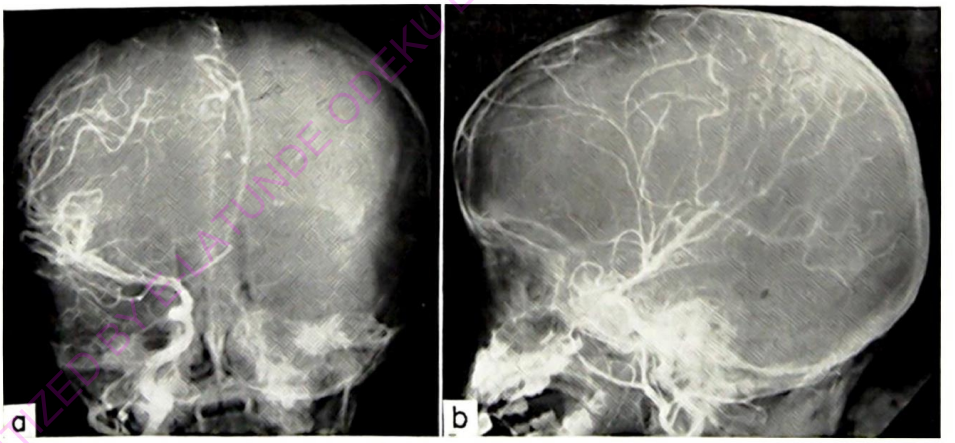

FIG. 1. Right carotid arteriograms (a) A–P view, (b) lateral view showing large avascular frontal area and shift distortion of anterior cerebral artery (cystic craniopharyngioma).

Case report

The unusual case of a 6-year-old Yoruba boy illustrates a bizarre presentation of a massive cystic craniopharyngioma. He was brought to the hospital as a 'mental retardation' problem, having become increasingly apathetic and incontinent of urine and faeces. For a period

of 1 month he had had vomiting and left Jacksonian seizures and had become markedly ataxic, bedridden and irrationally offensive in his manner and speech. Examination revealed papilloedema, left hemiparesis and positive Macewen's sign. Routine laboratory studies of blood and urine specimens were normal. Sutural diastasis was noted in the plain skull radiographs and right carotid angiograms (Fig. 1 a and b) revealed a large frontal lesion, the pattern of which suggested either an arachnoidal cyst or an abscess. Partial aspiration through a right coronal trephine gave 50 ml of bright yellow oily fluid (laden with cholesterol crystals) under significant pressure. At a subsequent craniotomy a massive craniopharyngioma sac with a blue hue was found occupying the entire right frontal fossa. The right frontal lobe had been markedly compressed far posteriorly into a deep concave-surfaced lobe. Only a very small portion of the suprasellar cyst extended over to the left side. The sac contained chocolate-coloured fluid at the second operation (altered fluid). Post-operatively, the patient has improved over several months, walking steadily, doubly continent and has been behaving acceptably.

Radiographic findings

Plain skull radiographs were obtained in all of the patients. With pituitary adenoma, seventeen showed enlarged and/or eroded sella turcica and double fossa contour was seen in one instance. There were frank acromegalic changes (increased skull thickness, extensive frontal sinus, etc.) in four. Supportive skeletal changes in the hands, feet and jaws were also noted. Intrasellar calcification was present in one instance. In two patients the skull radiographs were normal. All of the craniopharyngiomas showed abnormal changes in the plain skull radiographs. Five of the ten had calcifications (four suprasellar and one supra—and intrasellar); four had sutural diastasis and three enlarged sella turcica.

Cerebral angiographic studies in nineteen patients with pituitary adenomas showed normal vascular configuration in four. Diagnostic elevation and posterior displacement of the A-1 segment of the anterior cerebral artery was defined in twelve instances and was only suggestive of a suprasellar mass in two others. In one additional case the carotid syphon alone was elevated. All ten patients with craniopharyngiomas were studied angiographically and only one of them retained a normal vascular pattern. Four showed diagnostic displacement of the A-1 segment, and three had hydrocephalic configuration of the pericallosal arteries. Another patient showed both alterations in the vascular pattern. A massive shift of the main anterior arterial branches indicated a huge avascular right frontal mass in the eighth case which has been described above (Fig. 1a and b). This was an unusual angiographic pattern of abnormality for a craniopharyngioma in our clinic.

Result of operative treatment

Two of the pituitary adenomas and one of the craniopharyngiomas did not come to operation. All three of them died. Of the craniopharyngiomas, seven were found to be cystic, whereas only four of the twenty-two pituitary adenomas showed significant cystic portions, the majority being solid and fleshy in bulk. As much as 45 ml yellowish fluid was evacuated from a cystic craniopharyngioma in a 3-year-old boy and larger amounts were removed in the reported case. Except for the tapping of a craniopharyngioma cyst through a trephine in a patient who came to hospital *in extremis* after months of illness, and also trans-sphenoidal approach in two patients with solid pituitary adenomas and whose optic chiasms were found to be markedly or moderately prefixed at previous craniotomy, all of the patients (twenty

adenomas and eight craniopharyngiomas) received osteoplastic craniotomy. Radical or subtotal intracapsular removal of the solid lesion, with evacuation of cyst where present, was performed in each case. Post-operative irradiation therapy was not given as the facility has not yet been instituted in our hospital. All of the patients received supportive hydrocortisone and few had addition of thyroxine after operation. The surviving patients have been followed for upwards of 7½ years and the majority of them have benefited from removal of their tumours. One of the patients with cystic craniopharyngioma received a second craniotomy for what was believed to be a recurrence. The re-exploration revealed hydrocephalic third and lateral ventricles and a large pseudo-porencephalic extension of the left lateral ventricle. Table 2 shows the overall fate of all of the thirty-two patients. Of the eight who died, three did not receive operative treatment. One of the operated patients with pituitary adenoma died on the twelfth post-operative day from diabetic coma and two others from hypothalamic infarction, as did a craniopharyngioma patient who showed aggravation of hypothalamic dysfunction following craniotomy. Causes of death among the patients who did not receive operation were bronchopneumonia and massive haemorrhage within the neoplasm.

TABLE 2. Outcome in thirty-two cases of neoplasms of the sella turcica region

Result	Pituitary adenoma	Craniopharyngioma
Well	7	4
Improved	7	3
Died	5 (2 unoperated)	3 (1 unoperated)
Unknown	3 (2 improving)	–

TABLE 3. Thirty-two neoplasms of the sella turcica region—histologic types

Adenomas of the pituitary gland	
Chromophobe	15
Mixed eosinophilic	7
Mixed basophilic	—
Total	22
Craniopharyngiomas	10

Pathological considerations and tissue culture of the neoplasms

(a) The histologic components of the thirty-two tumours of the sella turcica region are shown in Table 3. Twenty-two of the pituitary neoplasms were adenomas of the anterior lobe (pars glandularis) of the gland. All of the twenty-two neoplasms had chromophobe cells and in seven of these there was an admixture of eosinophilic cells. Thus, fifteen (68·18%) of the neoplasms were pure chromophobe adenomas. No basophilic neoplasms was found in this series. The typical polygonal cells without cytoplasmic granules were readily identified in

the tumour sections. Granular orange Gram-positive acidophilic cytoplasm was present in some of the tumours. Fewer still showed some PAS-positive basophilic cells.

One of the solid craniopharyngiomas showed the so-called 'adamantinomatous' features. In the majority of the tumours the cyst walls were composed of sheets of stratified squamous epithelium. Much calcific deposits and occasional calcospherules were seen.

(b) Cytology and tissue culture studies of three chromophobe adenomas (Case Nos. 7–9) and one mixed eosinophilic–chromophobe adenoma (Case No. 10) were made. Case No. 7 referred to a 56-year-old man with 3 years' complaint of bitemporal hemianopsic defect. He had a normal sella turcica with a ruptured diaphragma sellae and a large greyish cellular, moderately vascular encapsulated suprasellar mass. The 45-year-old lady in Case No. 8 had headaches (for a few months), right optic atrophy, bilateral ophthalmoplegia and was in semicoma at the time of her admission to the hospital. Her sella turcica was enlarged and the clinoids were eroded. At craniotomy the greyish cellular neoplasm contained liquid blood and small dark clots. In Case No. 9, an 8-year history of amenorrhoea and infertility was obtained from the 31-year-old lady who also complained of frequent headaches, progressive obesity, loss of memory for recent events, olfactory hallucinations and bitemporal hemianopsic defects. The sella turcica was enlarged. A soft, thinly encapsulated cellular pituitary neoplasm was found at craniotomy. Impressive acromegalic features (including cardiomegaly), generalized headaches and early bitemporal hemianopsia were found in the 42-year-old man in Case No. 10. His sella turcica was quite large. The pituitary tumour was removed by trans-sphenoidal approach after craniotomy revealed a wholly prefixed chiasm and a broad aneurysmal dilatation of markedly displaced (medial-ward) carotid artery.

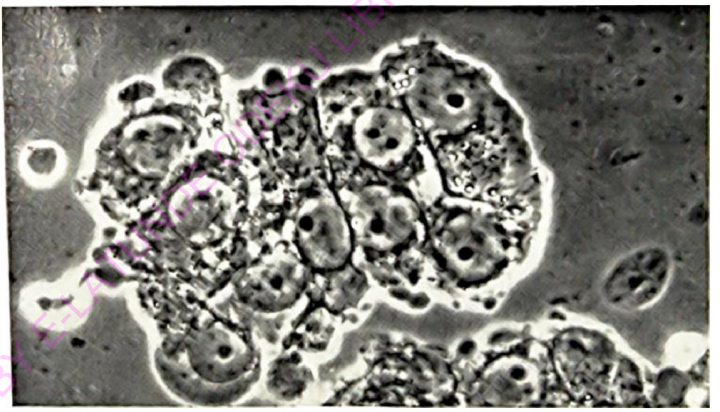

FIG. 2. Freshly dispersed eosinophilic adenoma cells. Variation in cell size is marked. Most nuclei contain single prominent nucleolus. Cytoplasm is abundant and granular. Phase, ×400.

Materials and methods (*cytology and tissue culture studies*)

Biopsies from four cases (Nos. 7–10) were collected in dry universal bottles and processed immediately. A portion of biopsy material was removed for preparation of touch (imprint) smears. The rest was immersed in 2 ml of medium 199 in a Petri dish and the cells dispersed by gentle teasing between a pair of forceps and knife. The dispersed cells were washed by

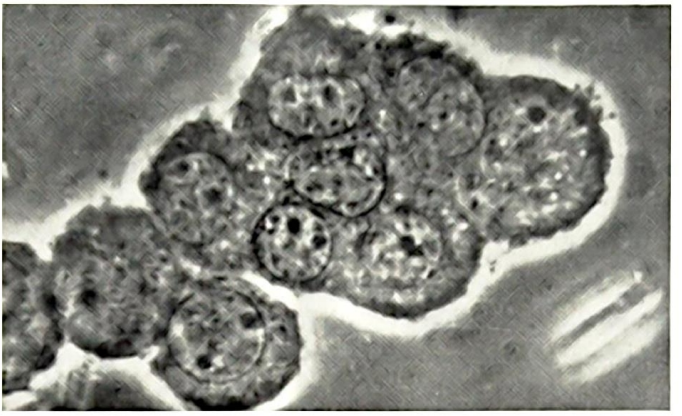

FIG. 3. Freshly dispersed chromophobe adenoma cells showing tight cohesion and chain formation. Nuclei contain more than one nucleolus. Cytoplasm is dark, agranular and scanty. Phase, × 900.

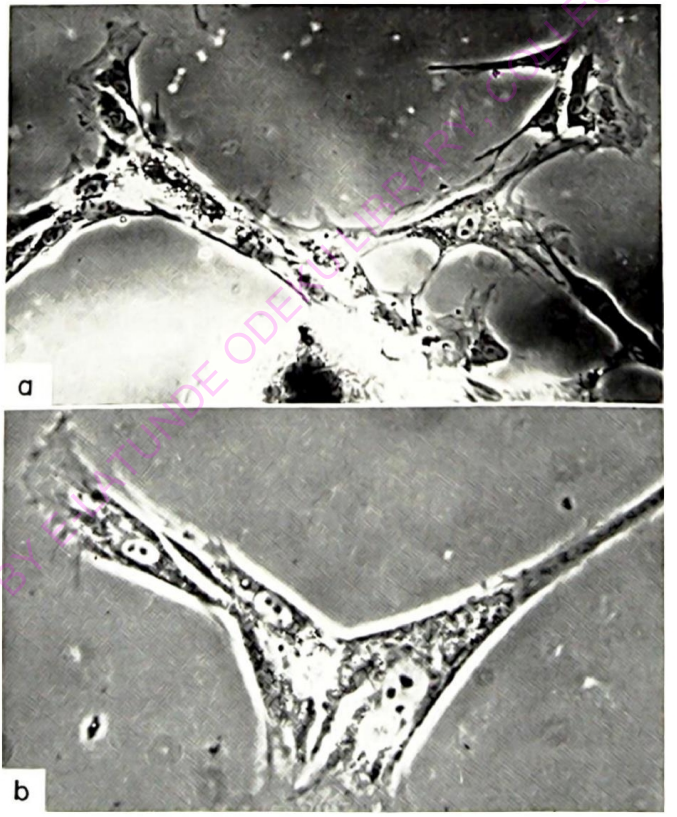

FIG. 4. (a) Chromophobe adenoma cells growing out as a monolayer from the edge of biopsy explanted 3 weeks earlier. Phase, × 100. (b) Higher magnification of cells showing finely granular cytoplasm. Phase, × 200.

centrifugation in two changes of 199 at 250 g for 5 min. Some of the washed dispersed cells were seeded on to agar roller slides and ring chambers as described by Pulvertaft (1965). The rest were resuspended in culture medium and incubated at 37°C as stationary bottle cultures. Culture medium was 30% human serum in 199, supplemented with 0·4% of chick embryo extract (Difco).

Chamber cultures were examined twice daily for survival and morphological characteristics of the cells. 1 ml aliquots of suspension cultures were removed on alternate days for phase contrast microscopy and stained-smear preparations. Smears were stained with May–Grunwald–Giemsa stain.

Results (cytology and tissue culture studies)

Case 7. Consisted predominantly of tightly coherent highly granular polyhedral cells. Survival *in vitro* was extremely poor, with no viable cell seen after 24 hr in culture.

Case 8. Yielded swarms of non-coherent cells with some variation in size. The cells were round and essentially monomorphic. The cytoplasm was abundant, agranular and contained a good number of round mitochondria present only in the juxtanuclear area (Fig. 2). The cells survived fairly well *in vitro*. There was tendency to clumping, although the cells showed no attempt at adhering to glass during the first 2 weeks. The cytoplasm became increasingly granular and opaque (Fig 3). Cultures remained viable for over 4 weeks. On the fifteenth day of culture, attachment to glass and spreading of cells was noted, and by the end of the third week a substantial number had flattened out on glass as monolayer cultures (Fig. 4a and b). There was no evidence of increase in cell numbers, although the cells remained remarkably healthy. The persistence of numerous minute spherules of mitochondria gave a dark granular appearance to the cytoplasm. The cells were readily distinguishable from 'fibroblasts' which are normally rapidly proliferating, have predominantly filamentous mitochondria, transplant, cytoplasm and are readily glass-adherent.

Case 9. Cytologic and *in vitro* survival characteristics were the same as in Case 8.

Case 10. The cells were tightly coherent, polyhedral and granular and showed rapid death *in vitro* similar to our experience with cells from Case 7.

COMMENT

In the Asiatic series of 3312 Japanese brain tumours (ICM) of Katsura, Suzuki & Wada (1959), there were 365 pituitary adenomas (11% ICM) and 240 craniopharyngiomas (7·23% ICM), giving a combined total of 18·23% ICM for both types of neoplasm. This is not far from the Cushing's (1932) rather high total of 22·4% ICM (17·8% for pituitary adenoma and 4·6% for craniopharyngioma). In their attempts to clarify some ethnic aspects of tumours of the brain Mosee, Barber & Earle (unpublished data) (1970) found the proportion of pituitary adenomas in the Black population in the record of the Armed Forces Institute of Pathology in Washington, D.C. to be 17·64% ICM as against 6·1% ICM in the White population (AFIP). They concluded, however, that 'in the overall average the increased incidence of this tumour in Blacks is slight, 9·41–7·93%'. A total of 5807 ICM was considered, of which 6·1% (or 357) was from the Negro population.

Olivecrona's (Hoessly & Olivecrona, 1955) series of 5250 brain tumours had 445 pituitary adenomas, a frequency of 8·5% ICM. The craniopharyngiomas were much fewer (below 3% ICM). Only 2·7% ICM of Zülch's (1967) 4000 brain tumours were cranio-

pharyngiomas and 7% were pituitary adenomas. The Asiatic Indian series of Dastur, Lalitha & Prabhakar (1968) gives a comparable frequency of 6·7% ICM (from 1000 masses) and 8·7% ICN (from 768 neoplasms) for pituitary adenoma.

These neoplasms appear to be more frequent in the African patients seen at Ibadan than in Caucasians, and this higher frequency is in keeping with similar findings among the American (U.S.) Negroes (Mosee *et al.*, 1970) and the Japanese (Katsura *et al.*, 1959). The series from Ibadan by Odeku *et al.* (unpublished data) (1970) constitutes 11·9% ICM (pituitary adenomas) and 5·96% ICM (craniopharyngiomas) of a total group of 134 intracranial masses of various histologic types. The combined frequency of 17·88% ICM being still higher than the 13% ICM of 1965 previously reported from the same medical centre by Odeku & Janota (1967). In the latest analysis of 186 Ibadan brain tumours (Odeku *et al.*, 1973) this high frequency persists at 17·20% ICM.

One notes the greater preponderance of the male to female ratio of 2 to 1 for craniopharyngioma found in the large series of Zülch (1967), there were nine males to one female in this series. Of their fifty-seven children with craniopharyngiomas Matson & Crigler (1969) had even sex distribution of twenty-nine females to twenty-eight males. In the Caucasian the craniopharyngioma age peak is from 13 to 17 years (Zülch, 1967). This range is a number of years older than that noted in Ibadan where seven of the ten patients were below the age of 10 years. Zülch also found the pituitary adenomas at their highest in the fifth decade which is again 1 decade older than in the patients at Ibadan.

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