

MELANOTIC INTRA-OCULAR SARCOMAS

A Report of Nineteen Cases. With
Two Post Mortem Findings.

A THESIS

Presented for the Degree of M.D.

by

Charles William Yow.

The Sect.

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IN adopting the term "melanotic sarcomas" I do not wish to imply that these tumours were necessarily mesoblastic in origin, but that the cases I am about to report and discuss are better known as such clinically.

This type of intra-ocular tumour is very rare indeed, as leaving out Cases I, XIV, XVII, and XVIII out of an average of 40,000 patients seen annually, only fifteen cases were seen in a space of five years.

I will not attempt to introduce any controversial matter in the already voluminous literature on the subject, but in presenting this consecutive series of cases, all of which I have personally investigated clinically or pathologically, I hope some important points may be elicited.

When I started this investigation, I had in mind the question of prognosis - to trace the end results of these cases. I found, however, my numbers were limited, and although only a space of five years was involved, it necessitated a good deal of work, and in a few cases actual visits to their homes, in order to get at a more accurate record of their cases. It was extremely fortunate that I was able to report the post-mortem findings in two cases.

In five cases of this series the results proved fatal, these died at an average time of about three years after enucleation, and all of these have definitely died from metastasis. Another two are at the moment under observation for "abdominal cancer" (one in bed), the other with metastasis in lung (shown by X-ray). Three others have clinical enlargement of liver, but no other signs of malignant disease.

The average age of my cases was 56 years (the youngest was 24, and the oldest 74 years). Lawford and Collins give an average of 48.42 years. Parker and Stokes report ten cases of intra-ocular sarcoma in children at average age of 3 years - some of these were bi-lateral, and all were non-pigmented - most of these, I believe, were so-called gliomas of the retina.

Both sexes were equally affected, and in no case was it bi-lateral.

Heredity: Recorded cases of "cancer families" are very remarkable. Cases II, V and VI gave suggestive histories. Much more definite results have been obtained by animal experimentation. Mendel Sly, experimenting on mice, found those immune behaved like Mendelian dominant character, whilst those susceptible behaved like a recessive. Parsons records cases of a mother and two daughters affected with sarcoma.

Trauma or chronic irritation: Several of my cases gave a definite history of trauma or previous incidence of chronic inflammation.

Dawson records a case of Prof. Wilkie, where generalised melanosis followed a scratch of a mole on the forehead.

Trettenero also published an interesting case of a child developing sarcoma following injuries to right eye, two months after. Ewing states that a process beginning as a simple inflammatory hyperplasia may in the same individual gradually assume neoplastic properties.

The mechanism by which injury induces tumour growth is generally obscure. Sarcomas have been known to follow on a single blow.

Clinical Features: Fuchs describes four stages in the development of sarcoma.

1) Pre-glaucomatous - a detachment of the retina with corresponding defect in the visual field - later a complete detachment with blindness.

2) Glaucomatous state - there is increase in the tension of the eye, and with the appearance of congestive Glaucoma - a painful eye.

3) Extra-bulbar extension with hard prominences in ciliary or equatorial region, or if the spread is posteriorly there is exophthalmus .

4) Generalised metastasis.

The detachment usually rises steeply from the surrounding fundus, and there is usually a brownish colour of the swelling. The choroidal or tumour vessels may be seen through the retina. If the detachment becomes complete, it is extremely difficult to be certain that we are dealing with a tumour.

The anterior ciliary veins may be dilated on the affected side or pigmentation may be seen at site of perforation of these vessels.

Terrien lays stress on the fixedness of the detached retina, together with the vessels seen under it and a raised intra-ocular tension which appears more slowly in growths of posterior segment than in those of anterior segment. Sometimes there is dilatation of pupil. Morax insists on scotoma and accompanying chorio-retinal changes. Foster Moore emphasizes the presence of stippling or vesicle-like bodies in overlying growth, irregular pigmentation - micropsia and scotoma.

Very few of my cases came up for examination, complaining of any definite symptom relative to an intra

ocular tumour. Several complained of failing sight or pain as a glaucomatous symptom, and detached retina was found only on routine examination of the eye. Others had blind painful eyes, as the result of long-standing inflammation, injuries, or were previously under treatment for some other cause.

The tension was raised in eight cases.

Diagnosis: I am not going to discuss details of diagnosis, or differential diagnosis, but will mention some important points.

The diagnosis of an intra-ocular melanotic tumour may be very simple or very difficult indeed. If the tumour is large and easily visible, whether in situ or by extra-bulbar extensions, it is simple. Only in ten cases was a definite diagnosis of tumour made in each case beforehand.

Transillumination is not possible when the tumour is situated behind the equator as a rule, and then one has to exclude a haemorrhagic exudation. Terrien recommends testing the resistance of sclera at site of the detachment with a small sound, or puncturing the site with a knife, or better still, with a needle and syringe, when the fluid can be examined for tumour cells.

Merigot de Treigny employs the slit lamp for trans-scleral and focal illumination - also for the investigation of anterior ciliary vessels and measurement of depth of anterior chamber.

In deep-seated tumours Mawas uses the binocular ophthalmoscope and contact glasses. E.E. Blaauw quotes Hertzell and Langenhams as using a strong light in post-nasal cavity to transilluminate posterior tumours and states that iridocyclitis, serous retinal detachment, vitreous haemorrhage, gumma, solitary tubercle and absolute glaucoma have all been mistaken for sarcoma of the choroid. In one of my cases, cysticercus was diagnosed. In another an iris pigmented cyst was mistaken for sarcoma.

Haemorrhages over the detachment were present in two of the cases.

Melanaemia and melaninuria seemed to be a variable feature - the former was not present in any of my cases, and in the latter condition two cases were suggestive. No abnormal cells were found on blood examination in these cases.

X-ray may be used with advantage as an aid to diagnosis, especially in cases showing extra bulbar extension with bony involvement of the orbit, or in secondary growths in lungs etc. (Case 19). It may be with improved

technique that it will be possible to show up an intra-ocular tumour by this means. I also tried it in case of the liver - of course on account of the more or less equal density of the tissues involved it was not possible to get a contrast shadow. A general enlargement of the liver was shown, however, in three cases.

Martin Grey tells me it may be possible to estimate some liver involvement by an indirect Graham's method. If this was so it will help us considerably in estimating the actual prognosis in these cases.

Wassermann should be done.

Situation of tumour: In about 17 cases the tumours were placed between ora serrata and posterior segment of the eye, and only in one case was the tumour definitely growing from the ciliary body.

Fuchs, Lawford and Collins found about 85-90% were in the choroid.

Pigmentation: All of my cases showed pigmentation, both macroscopically and microscopically. Case 17 showed a putty like tumour, but with a distinct band of pigmentation dividing the tumour. I believe the majority of intra-ocular choroidal tumours are pigmented, and this can be shown by serial sections. Stroud Hosford in his

unpublished series of 24 cases has found pigmentation in every case.

M. Knight quotes about 60% in the Mayo Clinic were pigmented.

Structure: The majority of these cases showed a fairly large tumour present on examination. How long have these tumours been present before they were recognised? It is extremely difficult to say, though in cases VIII and IX we may offer a speculation.

Melanotic sarcoma in the eye may show a remarkably wide difference in structure. The cells may be spindle, round, polyhedral or epitheloid, or a combination of any of these. One part of the section may show a sarcomatous appearance, and the other part side by side a carcinomatous appearance. The bulk of the cells in this series were of the spindle variety. In some cases it was possible that the sections being made at a different angle gave an altered appearance to the cells. It was extremely difficult to state definitely from which layer of the choroid were the tumours growing. The pigment was more or less evenly distributed or surrounding the vessels which were usually poorly formed. Mitotic figures were seen in practically all the cases. Boyd states the origin of these cells is not yet decided, and is still discursive.

Mary Knight thinks these are epithelial, as only these can produce melanin. She quotes B. Block and the Dopa Reaction with which the colour of cells of pigmented naevus and pigmented epithelium of retina is increased. On the other hand, the chromatophores of dermis and choroid do not give the reaction.

Dawson in his very excellent monograph states that pigment occurs normally in uvea, pigment layer of retina, posterior layer of iris and ciliary processes, sclera and at points of exits of anterior ciliary vessels and optic nerve sheath. He maintains it is epithelial in origin, and from the retinal pigment layer, and thinks there are two types of cells: the melanoblasts which form pigment and the melanophores or phagocytes. Ribbert maintains that different forms of cells are the development stages of the same cell - the normal chromatophore of the choroid.

Spencer thinks melanoblasts are epithelial in origin. Collins holds that melanoblasts may be either epithelial or mesodermic in origin.

Miss Mann from an embryological view argues it is mesodermic. Wagener and Wellbrock believe that in development the pigment epithelial layer of retina is split into two layers by ingrowing vascular tissues of choroid and therefore these tumours are epithelial in origin.

Sampson Handley maintains these are mesoblastic, and quotes Borst in support.

Smith by tissue culture has shown that pigment can be produced by epithelium or connective tissue.

Metastasis - occurs rapidly if growth has extended extra-bulbar. The internal organs are usually affected. In generalised metastasis, secondary growths may be found in liver, lungs, kidneys, thyroid, heart, pancreas, brain, skull, vertebrae, orbit, lymph glands. The amount of pigmentation and the type of cells in the primary may not be reproduced truly in the secondary deposits.

Letchworth told me of a case where the eye was removed for a melanotic sarcoma developing carcinoma of intestine later on.

Mode of spread is by emboli and blood stream, lymph spaces, and by exits of perforating vessels and nerves, and optic nerve sheath. Sampson Handley maintains that chief mode of spread in melanotic sarcoma is by lymphatic permeation, and secondarily by blood stream. The lymphatics in the orbit are imperfectly known (Whitnall), and so this mode of spread may not be so common as in melanotic sarcoma in other parts of the body - sections of case II show perivascular and perineural extension.

Prognosis: If the tumour has extended extra-bulbar, it is an extremely fatal disease. Melanotic sarcoma tends to metastasised very early, or it may be years after. Of all my fatal cases every one developed metastasis.

The tumour emboli show predilection for certain organs—great numbers are presumably killed off in the blood stream and this may account to a certain extent for the delayed metastasis. Sampson Handley, Schmidt and others have shown that the blood has a destructive action on cancer cells.

Foster Moore quotes a case in which metastasis occurred seventeen years after enucleation of the primary growth.

Treatment: If it is possible to diagnose early and the eye removed, it is very likely the results will be favourable. On the other hand it is so difficult to estimate how long the tumour has been in existence, and to determine the presence of metastasis, that it may be advisable to exenterate the orbit in every case, as it will be nearer to the surgical ideal adopted in cases of melanotic tumours elsewhere. Exenteration should be performed in extra-bulbar extension. In either case it may not prevent metastasis.

Surgical diathermy may be tried with advantage. Radium for recurrent cases, extra-bulbar extensions, or together with exenteration, may be useful.

Conclusions.

1) That melanotic sarcoma in the eye is a fairly malignant tumour, and it occurs usually in the "cancer decade" of life.

2) It is invariably pigmented, and is usually of the spindle cell type, but may be of mixed celled variety.

3) That a fair number of cases of this condition are diagnosed accidentally in the laboratory (Terrien quotes "at Moorfield, out of 82 cases enucleated for absolute glaucoma, 50% were sarcomas, and these were not diagnosed beforehand"), and so there is room for improvement in our diagnosis.

4) That every blind eye of unknown cause, and where the fundus cannot be examined, should be enucleated and examined macroscopically and microscopically. All enucleated eyes should always be thus examined.

5) That the use of radiograms may be helpful in the diagnosis of the primary as well as the metastasis in this condition.

6) That the tumour is usually large in size when first seen, and in view of the uncertainty as to the time of its existence, it may be prudent to exenterate the orbit in every case of intra-ocular melanotic sarcoma.

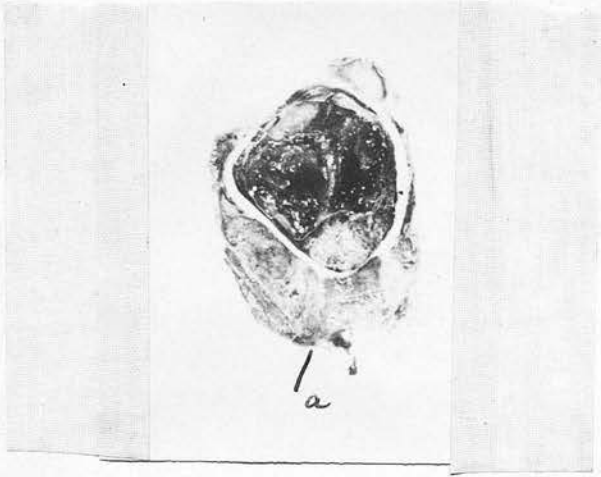


Fig. I. Shows extra-bulbar extension (case I.) (a)



Fig. 2. Shows a large tumour involving about one half of the globe. (Case 13). X.

Case I. William E-- , aged 27, coal porter, was sent up to Hospital with proptosis, etc. R.V. = 6/5, L.V.

Left eye was removed on 15.2.1917. Very scanty clinical notes were available.

Specimen showed a large pigmented tumour spreading out from nerve head and gradually thinning out towards ciliary region. There was a larger extra-ocular extension surrounding posterior pole of the eye.

Microscopic examination: Tumour is of well defined spindle celled type - attempt at whorling - nucleus stains rather badly. Pigment scattered throughout tumour and mostly around vessels which are poorly formed - some mitosis present.

Mrs. E-- wrote on 17th September 1931: "Very sorry to say, but Mr. William E-- has been dead this fifteen years, died with cancer on the liver."

Case II. Mrs. Mary G-- , aged 63, a gold and silver burnisher.

This patient first came under observation in 1927 when she applied for presbyopic glasses. It was then

PLATE II.

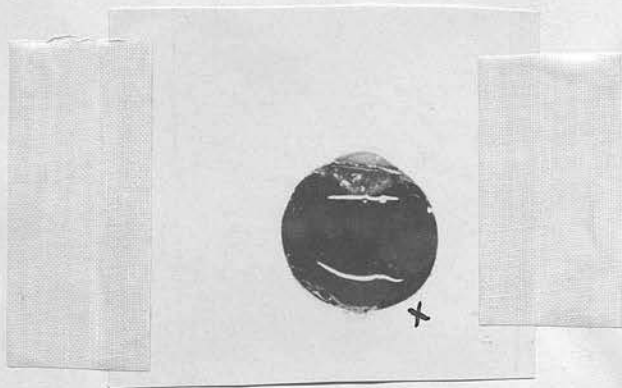


Fig. I. Shows a comparatively small flat tumour (case 2).

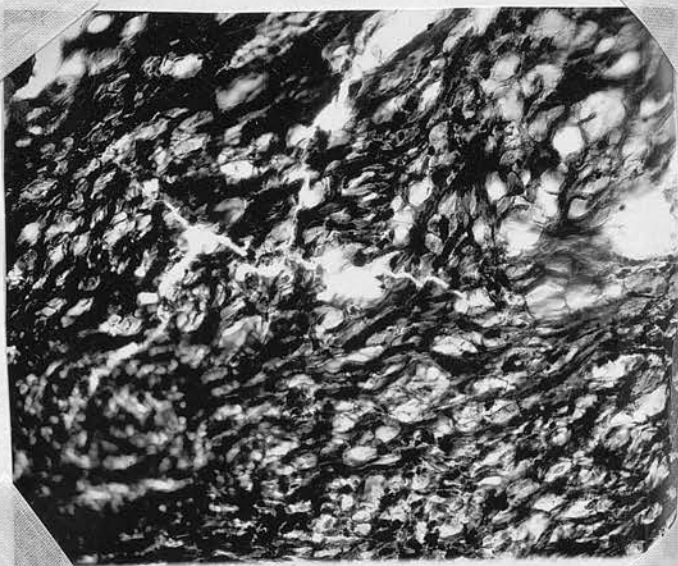


Fig. 2. Section showing type of cells and peculiar spaces (Case 2).



Fig. 3. Section shows spaces as in fig. 2. and embolus of tumour cells in a scleral vessel (x). Case 2.

noticed that she had a shallow swelling of the retinae involving the central area. Her vision was then 6/9 partly with correction and tension was normal. She was subsequently seen by several oculists and there was a diversity of opinion as to whether the prominence was of a simple or malignant type. In a few weeks there was some loss of vision to 6/18, and there was a globular swelling about the macular area and above and about the size of a small almond nut. T.N. No external dilatation of vessels. L.V. with glasses = 6/6 most. The right eye was enucleated 10.11.27. The specimen showed a flat pigmented tumour occupying posterior 1/3rd of globe about 7 mm. long. No extra-ocular extension was noted. There was a detachment of the retina.

Microscopic Examination: Tumour consisted of polyhedral cells with tendency to spindle - marked pigmentation in parts - numerous clear spaces, irregular and varying in type (probably artifact) with ragged wall composed partly of sarcoma cells and partly of fibrous tissue without epithelial lining. Not much haemorrhage. No extra-ocular extension noted. The general appearance is that of a fibro-sarcoma type.

She was next admitted into Hospital on 25.6.31, complaining of pains in stomach, weakness, and incapable of taking food.

Family History: Mother died of "yellow jaundice".

History: At 24 years old, had "ulceration of inside". About six weeks ago felt a pain in right side over chest.

Respiratory System: Movements good and equal.
V.F. and P.N. normal.

Cardio-vascular System: Apex beat not palpable. Heart not enlarged to percussion. Heart sounds: first sound at apex rather slapping in character. Both sounds well heard over all areas.

Alimentary System: Spleen not palpable. The liver is enlarged a hand's breadth below costal margin, but is not tender.

Complains of sickness, and is taking only milk and biscuits.

Central Nervous System: Knee and ankle reflex present. Plantar reflex is flexor.

Left eye reacts to light and accommodation. Marked yellow tint on sclerotic.

Weight: 7 stone, 9 lbs.

Temperature: About 101⁰ for about one week; then 98⁰ at death (12th July 1931)

Pulse: 120/116/106/116/100/104/ etc.

Urine: Daily quantity diminished. Melanin - none detected. Urobilin and urobilinogen - present.

Patient died on 12th July, 1931.

Post-Mortem Findings:

Melanotic tumours were found in liver, kidneys, heart, skull and vertebrae.

Body: slight icteric tinge.

Thorax: Heart: valves: some atheroma of aortic. Coronaries show slight atheroma. A few small black nodules in wall of right auricle and ventricle. There were none in left heart.

Pleura and Lungs: Old adhesion at R. apex. Both lungs were oedematous and right lower lobe was collapsed.

There was nothing of importance to record in tongue, thyroid, tonsils, trachea, oesophagus, large and small gut, pancreas, suprarenals, bladder and uterus. The liver was enormous. The upper surface was on a level with upper border of 3rd rib. Most of hepatic tissue was replaced by nodules of growth varying in colour from white to black.

Gall-bladder contained one small cholesterin stone.
The mucous membrane of strawberry type.

Kidneys: a few deposits of growth towards both renal pelvis.

F. Tubes and Ovaries: Tubo-ovarian cyst on left side, size of grape-fruit. No intra-cystic growth.

Glands: Upper abdominal and portal glands were invaded by growth.

Brain: Nothing to record.

Skull: Several deposits of growth in diploë - both tables were destroyed in parts.

Vertebrae: Scattered small deposits were present.

Right Femur: No evidence of growth.

Right Orbit: No local recurrence was found.

Microscopic Examination:

Scattered foci of melanotic growth containing pigment in glands. There was diffuse infiltration with similar growth in liver and skull. The heart muscle showed deeply pigmented nodule of similar growth. The right optic nerve showed signs of atrophic changes.

PLATE III.

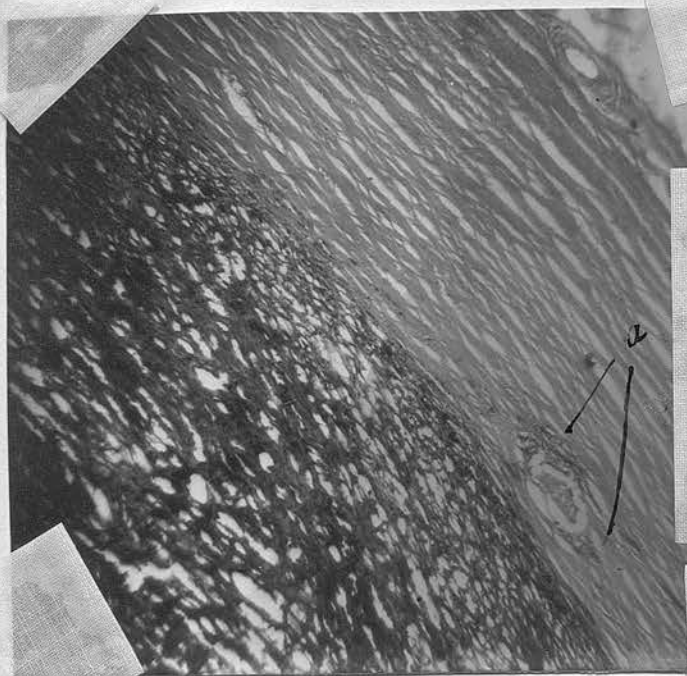


Fig. 1. Section shows perineural and perivascular invasion. (a)
Case 2.

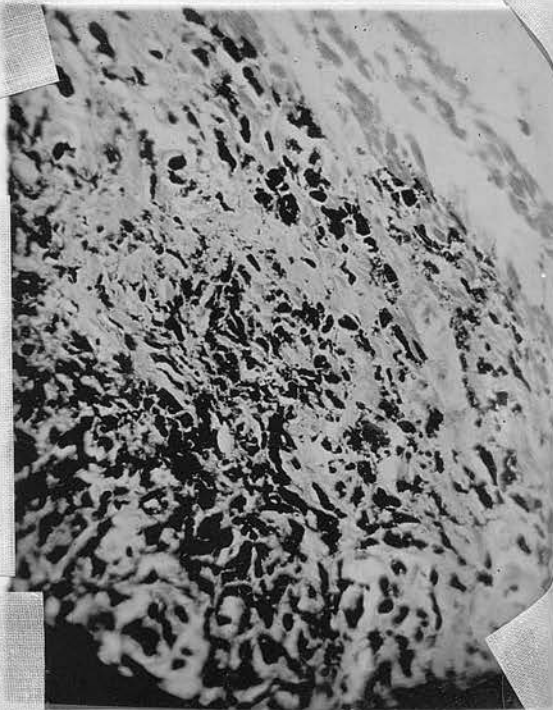


Fig. 2. Section through muscle showing pigmented metastasis. Case 2.

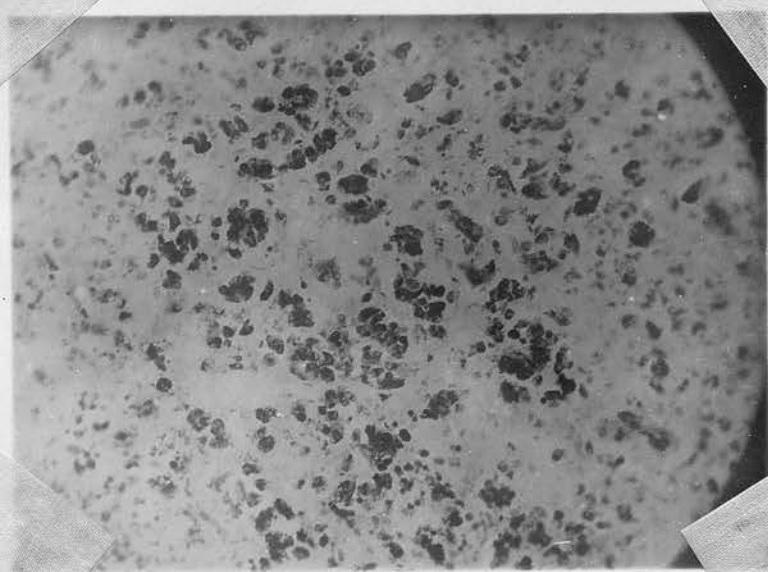


Fig. 3. Section through liver showing extensive destruction of liver tissue. Case 2.

The later clinical history and P.M. findings were compiled from particulars furnished by the Middlesex Hospital and Bland-Sutton Institute.

I examined sections of the liver and heart muscle, with the following result:

Heart Muscle - small nodule consisting of deeply pigmented cells with tendency to spindle form and with small amount of fibrous stroma - more or less circumscribed, but there is invasion of muscle tissue in the periphery.

Liver - the liver tissue is disorganised by growth - few small strands and isolated liver cells recognisable. Tumour cells occur singly or in small masses - the majority of which are pigmented, often very deeply. Some of the larger masses of cells show tendency to spindle form and are pigmented - though the larger proportion of these are devoid of pigment.

Case III. Mrs. Henrietta M--, aged 45, housewife, came up on 3.12.1920 to hospital, with a history of failing left sight for last 7 months. She also stated that she fell "downstairs" some two years previously. R.V. 6/9 F.N. L.V. = hand movements - tension normal. There was a circumscribed circular detachment up and out (mostly outwards), surface of which was covered

with haemorrhages. It looked solid, but trans-illumination was negative. She was seen again on 7.1.1921. The size of the detachment had not altered, but there was a fresh larger haemorrhage on its surface above. On 4.2.1921 the detachment appeared larger and there were more haemorrhages - tension of the eye was normal and there was no pain.

The left eye was enucleated on 2.3.1921, and a growth was found on bisection. It was deeply pigmented and growing towards the ciliary region, and posteriorly involving practically half of globe, about 15 mm. long and 14 mm. thick. No extra-ocular extension noted.

Microscopic Examination:

Cells were densely packed with well-marked nucleus of vesicular type-cells mostly of spindles but in parts are of polyhedral type. Very little stroma. There was fair amount of mitosis. Brownish pigment scattered throughout sections more or less evenly. Vessels were poorly formed and few of these showed definite

invasion. No haemorrhages seen.

Teased specimen:

Cells were of small spindle and others more pear shaped.

She was next admitted into King's College Hospital on 28.12.1925, and died on 12.4.1926 with general metastasis.

On 28.12.25 she complained of lump in stomach and dyspnoea - noticed the lump 8 months previously and it has been growing larger recently. She also noticed she was losing weight for some time. Dyspnoea present for 4 weeks, together with a loose cough. Bowels were regular. There was no difficulty in micturition, and no vomiting. She was married when 40 years old, and has 2 children. The left eye was removed at the Royal Eye Hospital three years ago. Relations were all well and healthy. A brother died from "heart trouble".

Present condition: Patient looks ill and wasted -
dyspnoea bad, and is weak - breath foul - temperature
normal - pulse 96.

Blood: R.B.C., 3,176,000 per c.mm.
W.B.C. 8,000 "

Respiratory System: Diminished movement of L.
side, especially at base. Dulness at both bases,
especially behind and on left side. Crepitations at
bases.

On 18.1.1926 the abdominal swelling was increasing
in size. Lower edge of liver descended to 1" downwards
in the last fortnight. There was tenderness in flanks.

The abdomen was distended irregularly by a hard
swelling which was more marked in R. Iliac and umbilical
regions. The tumour extended from under costal margin
above on both sides, filled right flank and most of
left, and reached downwards IV fingers' breadth below
umbilicus. There were big glands in inguinal and
axillary regions.

Heart: pulsation weak. Pulse volume and tension
good.

On 18.3.1926. Ascites was present. Oedema of
feet. Abdomen enormously distended. Liver increased in

size - was large, nodular and irregular on surface - reached to the pubic crest in front.

Urine: showed trace of melanin on 13.2.1926.

Van den Berg reaction: showed no liver damage on 29.12.1925.

Ascitic Fluid: no malignant cells - lymphocytes, endothelial, polymorphs, and red blood cells. Some cocci in direct smears.

Patient died on 12.4.1926.

Post-Mortem Findings:

General condition: Very wasted - legs were oedematous - oedema extending on to abdominal wall anteriorly.

Pleurae: Nodule posteriorly on parietal pleura of left side.

Lungs: Umbilications on surface of both. On section many nodules were found throughout substance. Patch of congestion at L. base. Bronchial glands were normal.

Thyroid: enlarged and riddled with nodules.

Pericardium: Nodule on upper surface of diaphragm - some free fluid.

Heart: Nodules on outer wall and scattered throughout muscle - nodulated growth projecting into Rt. auricle. Many of these growths are just under endocardium and are pedunculated. Valves were normal.

Peritoneum: Adhesions general throughout abdomen. About 1 pint of yellow fluid.

Liver: Many adhesions to lower surface of liver - weighed 23 lbs. 3 ozs. Large white masses almost replacing liver tissue and compressing the little that is visible. In places the nodules show the dark melanin pigment. The liver extends nearly down to Pelvis and occupies nearly the whole of abdomen.

Spleen: $15\frac{1}{2}$ ozs., large and firm - no nodules seen. One nodule seen on an accessory spleen.

Pancreas: Firmly adherent to liver. Large, many nodules - pigmented patches are almost black.

Kidneys: nodules on both kidneys and throughout substance. The left showed some inflammation and a pigmented nodule on surface.

Urinary tract: normal.

Brain: Excess of fluid, especially under Pons and Cerebellum. Brain rather softer than normal. No secondary seen.

Uterus: Fibroma on surface - also secondary nodules. Pigment granules on back of broad ligaments and on ovaries.

Microscopic Examination:

Spindle-celled tumour of melanotic type arranged in carcinomatous manner - growth is sarcoma.

Tissue examined were: L. Kidney; R. Lung; L. Orbit Axilla; Heart and Thyroid.

Case IV. Mrs. Kate F--, 59 years old, housewife, was seen on 15.4.1926, and complained of failing sight for 4 previous months. L. eye became bloodshot.

R.V. = 6/12. T.N. - Left Eye was soft. Vision = P. of L. There was detachment of retina on temporal side. O.D. normal. On trans-illumination, temporal quadrant was not clear. Severe pyorrhoea present.

Family History: Nothing to record.

The Left eye was removed on 29.4.1926. The tumour was deeply pigmented, filling up about 1/3rd of globe from ora serrata and extending posteriorly, about 13 mm. long and 10 mm. thick. It was very

PLATE IV.

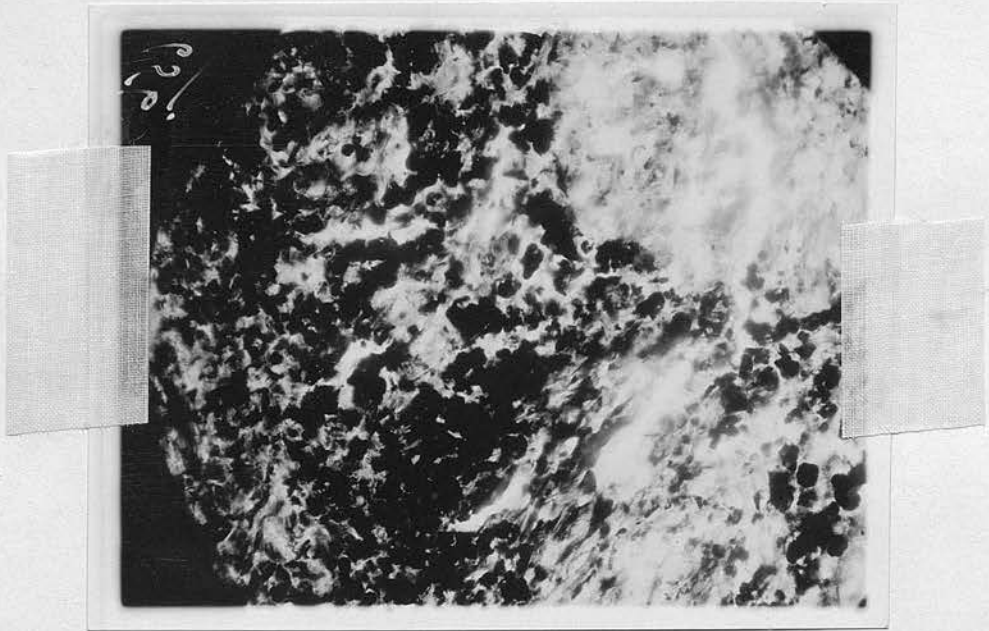


Fig.I. Section showing deeply pigmented tumour(Case 4)

vascular and haemorrhagic, and consisted of masses of spindle cells with large nuclei filling up the cells. Few mitotic figures were present, and fair amount of pigmentation. The pigment was numerous in neighbourhood of vessels and these were badly formed. Haemorrhage into tumour and some invasion of vessels noted.

No extra-ocular extension.

This patient was seen again on 11.9.1931. The left socket was clean. No signs of local recurrence. There is freckling of skin over chest anteriorly and posteriorly. Her general health has been good since the operation. Abdomen and chest: nothing to record.

Blood: No melanin or abnormal cells seen.
Lymphocytes 26%; Polymorphs 65%; Eosinophils 3%; Large Mononuclears 6%.

Urine: No melanin present.

X-ray of Chest and Liver: nothing abnormal noted.

Case V. Henry S--, 72 years old, builder's handyman, came under observation on 7.12.1926 for glaucoma in each eye. The right eye has been blind some ten years. No. P. of L.

On 8.12.1926 Herbert's sclerotomy was performed on right eye. There was iris prolapsed the next day and

it was excised. The R. eye was subsequently enucleated. Urine showed no melanin present.

On bisecting the eye, a large choroidal growth was found filling up half the globe, and with detached retina. Not much pigmentation. It was growing forwards and towards lens and ciliary region. No extra-ocular extension noted. The tumour was a spindle-celled sarcoma - cells diffusely arranged with very little tendency to whorling. No mitosis seen. Fairly vascular and vessels badly formed - most of cells were non-pigmented. No extra-ocular extension or invasion of vessels noted.

He was seen about 19th September 1931. Socket clean - no local recurrence. L.V. - 6/12.

Gastro-intestinal: nothing to record.

Abdomen: flabby - no fluid - no palpable tumour. Has been in very good health since operation.

Family History: Nothing to record, except one sister had her breast removed for accident when she was 59 years old, and died from the operation a year after.

Blood: No melanin or abnormal cells. Lymphocytes 39%; Polymorphs 62%; Eosinophils 4%; Large Mononuclears 1%.

Urine: no melanin.

X-ray of chest and abdomen: Calcified ribs and root glands right and left side. Liver showed enlargement, probably due to posture.

Case VI. Miss Elsie C.--, 58 years of age, housewife, came up to Hospital on 15th November, 1929, on recommendation of oculist. About a week previously she noticed a black shadow coming over right eye, and went to an optician, who referred her to the oculist. There was no pain, but a shadow when she looked upwards. R.V. = 6/9 and J., with glasses. L.V. = 6/9 and J., with glasses.

There was a brownish mass growing from ciliary body or adjacent choroid at lower inner quadrant of right eye. A detachment of retina which was non-translucent.

Had gastro-enterostomy 6 years ago, and can eat anything now.

Family History: Father died from nephritis and Mother from tumour of the bladder. 2 brothers and 3 sisters (one died from arthritis and another had retinal haemorrhages).

The right eye was enucleated on 19.11.1929. A pigmented tumour was found, 10 mm. long and growing from ciliary region and backwards to equator.

The tumour was spindle-celled sarcoma-pigmented - some of the cells looked round or cubical - most likely due to section being made transversely. Tumour dissecting up inner layers of sclera and also involving ciliary body and lig. pectinatum. No extra-ocular extension - a good deal of whorling - badly formed vessels. Similar type to that of T.J. and J.K. but more cellular. In parts of sections tumour undergoing hyaline degeneration. Very few mitoses.

She was seen September 1931. There was not much pigmentation of skin. Has had good health since operation. The liver is definitely enlarged. No fluid in abdomen. No history of jaundice.

Urine: no melanin.

Blood: No melanin or abnormal cells. Polymorphs 66%; Eosinophils 1%; Large Mononuclears 3%; Lymphocytes 30%.

X-ray of chest etc: liver enlarged. Calcification of ribs and root glands.

Case VII. Mrs. Louisa A--, 72 years old, housewife, was first seen in Dec. 1926, suffering from Iritis R. eye - post-synechial. In 1929 R.V. \bar{c} glasses = 6/18. L.V. \bar{c} glasses = 6/60. Left eye became inflamed in December 1929. Synechial ciliary injection and tension raised. A month later the eye was painful - tension raised. Vision = P. of L. The left eye was enucleated on 20th Jany., 1930. A deeply pigmented tumour was found growing from ciliary region and ora serrata and forwards into vitreous cavity. There was a good deal of pigmentation throughout - very vascular and little stroma, haemorrhagic - very little mitosis - vessels badly formed. No extra-ocular extension - difficult to state from which layer of choroid the tumour was growing - mostly small spindle type of cells.

In parts tumour was undergoing degeneration - some invasion of vessels by tumour cells.

She was seen in September 1931.

Family History: nothing to record. She has had good health since operation. Not constipated. Not much skin pigmentation.

Chest and gastro-intestinal: nothing to record.

Blood: no melanin or abnormal cells. Polymorphs 72%; Lymphocytes 26%; Eosinophils 1%; Large Mononuclears 1%.

Urine: no melanin.

X-ray Chest etc: R. and L. Nothing to record - there is a broad mediastinal shadow which is present sometimes in any metastasis.

Case VIII. Miss Ethel P--, 24 years old, clerk, came under observation on 20.3. 1925.

Previous History. Attended in June 1910 for refraction under atropine. R.V. = 6/9, L.V. = 6/9. Glasses were ordered. In March 1915, her glasses were broken and these were replaced after examination under atropine.

Family History: Nothing to record.

Present Condition: Early in 1925 noticed brown spot in front of R. pupil. This gradually got in front of centre and affected her sight. Her friends had previously advised her to seek advice. She thought she had it at least 3 years before she sought advice about it.

On examination: L.V. \bar{c} glasses =6/6. A small deeply pigmented growth was noticed growing from ciliary region and displacing lens backwards and filling up A.C. and growing across pupillary margin which was well defined. Tumour only seen on dilatation of pupil. Iris tissue over tumour is thin, and the deeply pigmented tumour showing through it. No extra-ocular extension.

The Right Eye was removed on 25.3.1925. The cells were spindle shaped and tendency to whorling. Fairly vascular - thin walled vessels - very deep pigmentation around vessels, but scattered throughout the tumour - no haemorrhages. Some invasion of vessels noted - Some small round cells present - No extra-ocular extension.

She was seen in September 1931 and is working again as a clerk. Since operation has had no chest, gastro-intestinal or urinary disturbance. One very deeply pigmented spot on left breast (present since birth). She is a bit constipated.

Blood: No melanin and no abnormal cells.
Lymphocytes 27%; Polymorphs 69%; Eosinophils 1%;
Large Mononuclears 3%.

Urine: No melanin.

X-ray Chest etc: Increase root shadow. No evidence of secondary.

Case IX. Mrs. Mary E--, 72 years of age, housewife. Attended in 1923 for defective vision. R.V. = 6/18. L.V. = 4/60. R. and L. lental opacities under treatment with Gutt. Sod. Iodid. until 9.6.25, R.V. = 6/18, L.V. = 3/60. Patient had severe pyorrhoea On 22.9.1925 left combined extraction of lens was performed and after that L.V. c̄ glasses = 6/18. On 15.12.1925 L. Capsulotomy and attended regularly every 3 months until 14.6.1927 when left detachment of retina was noted. It was upwards and obscuring 1/2 of optic disc.

On 26.3.1928 R.V. c glasses -- 6/18, L.V. c̄ glasses = 6/60. She attended regularly every month until May 1930, when L. eye was painful and tension raised. In June 1930 L.V. = no P. of L. - very painful, and the eye was removed on 11 June 1930.

There was a small pigmented tumour the size of a hazel not covering O.D. - fibrinous exudation in front of this. No sign of perforation. The tumour was fairly vascular and consisted of spindle type of cells - pigmented throughout. Some whorling. Vessels badly formed. Haemorrhages. Invasion of nerve-head - optic

nerve atrophy - parts of tumour undergoing hyaline degeneration. She was communicated with in September, 1931, and is well and about.

Case X. Thomas J--, 39, door-porter, came up on 7 July, 1931, complaining of painful right eye.

Previous history: was hit in the right eye about June 1924 with soldier's cane - no pain and no discomfort, but when he went up to rejoin the army a few months later it was discovered he had a detachment of retina. The eye was quiet until 6th July 1931, when it was bloodshot and painful.

Family History: Nothing to record.

On examination: The eye was tender - injected and a calcareous lens was in A.C. No P. of L. Tension raised. L.V. = 6/5. The right eye was removed on 8.7.1931. A small thick pigmented tumour was found, spreading from O.D. into vitreous cavity, and anterior half of eye, - size of a hazel nut - pigmented. Tumour cells were spindle shaped in parts and definite whorling. Scanty cytoplasm. Cell nuclei deeply stained - not much mitosis seen - pigment scanty in most of the tumour. Vessels numerous and fairly well formed - fair amount of stroma. No extra-ocular extension. In parts cells not so spindle shaped.

He was seen in September 1931, and has kept well since operation. No abnormal skin pigmentation. No enlargement of liver.

Urine: ? trace of melanin.

Blood: No melanin or abnormal cells. Polymorphs 60%; Lymphocytes 35%; Eosinophils 1%; Large Mononuclears 4%;

X-ray Chest etc. Nothing to record.

Case XI. Frederick C--, 67, carman, came up on 31.12.1930, complaining of loss of vision over one month. The sight has been misty for three months. No pain. No history of trauma.

On examination: R.V. 5 glasses = 6/12. Media clear. F.N. Tension normal. Teeth very bad. Left eye: detachment retina below - transillumination dull downwards and inwards.

On 12th January 1931 L. eye was removed. A pigmented tumour 10 x 12 mm. extended from ora serrata back to posterior part of globe and pushing retina in front of it. No signs of perforation. Cells were mostly cubical with large nucleus and nucleolus. Pigment sparsely distributed - fair amount of mitosis

PLATE V.

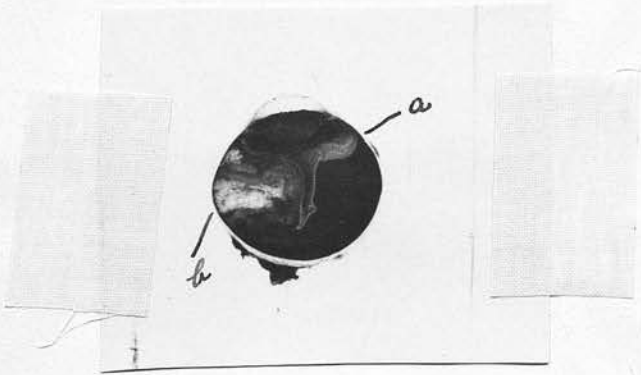


Fig. I. Shows an umbrella detachment (a) of the retina and a mushroom tumour. (Case I2).

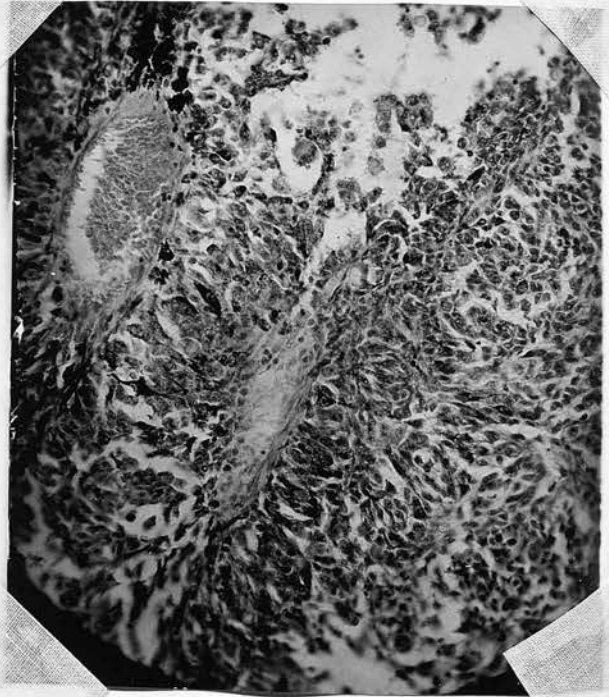


Fig. 2. Section shows thin walled vessels and different types of cells. (Case I2).

Vessels were poorly formed - there are a few spindle type of cells. Inner layers of sclera were infiltrated. Patient has since been under observation and treatment for "cancer of the gullet" and is now fed through a tube. This information was sent to me by his wife.

Case XII. Mrs. Elizabeth O--, 74, came up on 22nd July 1930, with a detachment of retina, right eye. The right eye was removed 23.7.1930.

Previous History: Had cancer of tongue and was treated with radium for 3 weeks with very good results. No scar - no restriction of movements. Glands were removed from Neck in December 1930.

The tumour in eye was fairly large, about 10mm. long and 12 mm. thick, and growing inwards. Fair amount of pigmentation - no extra-ocular extension. Tumour was growing from ciliary region backwards to posterior globe. The cells were polyhedral, showing radial distribution around vessels. Vessels were numerous and mostly of endothelial lining only. Cells showed moderate amount of cytoplasm and moderate sized nucleus with tendency to vesicular type. Fair amount of mitosis - pigment scanty throughout, but there are few deeply pigmented cells. In other parts are definite spindle cells. Inner layers of sclera infiltrated.

"This patient died in August, 1931, from cancer."

Case 13. Mrs. Jessie V--, 71, old age pensioner, came up on 27th January, 1925, with defective sight in each eye.

On examination: R. V. = P. of L - tension normal lental opacities. No history of tranma. There was a detachment of retina . Transillumination dull below and inwards. L.V.- count fingers tension normal - lental opacity.

On 12.2.1925, R. eye painful and transillumination dull - tension raised. R. eye removed on 7.4.1925. There was a large pigmented tumour involving posterior half of eye growing from choroid - Funnel shape detachment of retina - no signs of perforation. Size of tumour 20 x 9 mm. Cells were of spindle type, with whorled arrangement - very little stroma - number of badly formed vessels. Most of tumour lightly pigmented. Fine pigment granules in majority of cells and scattered irregularly and sparsely throughout tumour - not much mitosis - inner layers of sclera infiltrated. In September 1931, her daughter wrote "I regret to tell you my mother died 22 months ago from cancer of stomach"

Case XIV. Mrs. Bessie N--, 49 years, housewife, attended hospital on 8th June, 1928, with history of progressive dimness of vision in right eye for past three months. Eyes good movements.

PLATE VI.

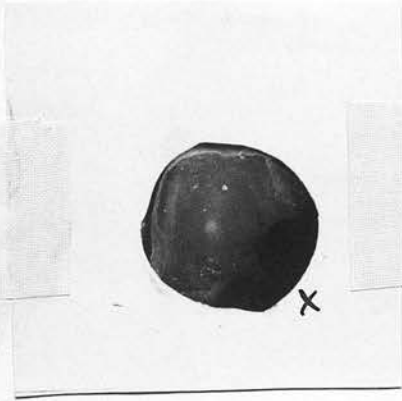


Fig. I. Specimen shows a deeply pigmented tumour. (Case. I4). x.

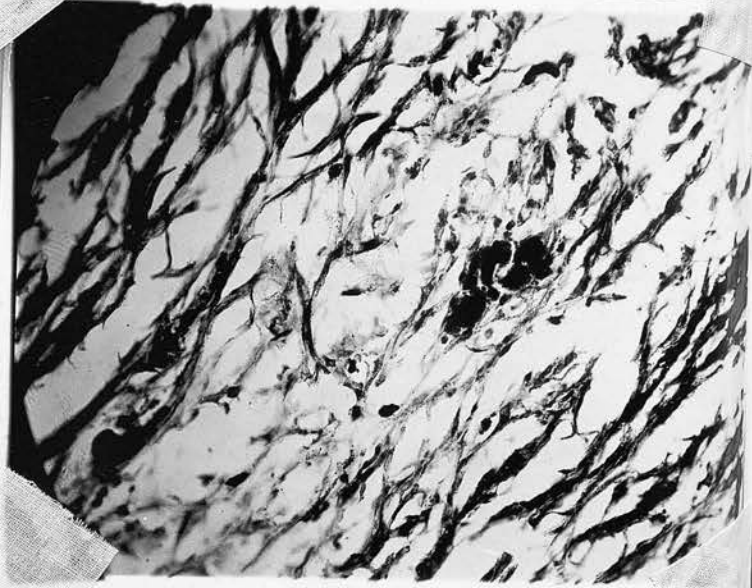


Fig. 2. Section showing elongated spindle cells and irregular spaces. (Case. I4).

On examination:

Abdomen)
Heart) Nothing abnormal discovered.
Lungs)

No enlarged glands in any part of the body.

Right eye: Large ciliary staphyloma - dark mass at upper periphery of A.C. - Iris very dull - No red reflex - Iris pigment on lens capsule - no P. of L. Tension distinctly up.

Left Eye: V = 6/6. Tension normal.

The right eye was removed in June 1928. There was a deeply pigmented tumour (coal black) about 10 mm. broad and 4 mm. thick from ora serrata to equator. No signs of extra-ocular growth. There was a good deal of pigmentation and tumour consisted of elongated spindle cells with small nuclei in which no nuclear structure can be made out. The histological details are obscured by the very deep pigmentation. Very few vessels present - much more adult type of cells - Scleral vessels involved with pigment and tumour cells. Inner layers of sclera infiltrated.

Up to September 1931 patient was alive and well.

Case XV. Thomas C-- , aged 54, wood-sawyer, came under observation on 22.6.1931.

Previous history: Gastric trouble for last 4 years. Has always been exposed to injuries by flying bits of wood; but never had any serious one to cause him to seek advice. About $3\frac{1}{2}$ years ago found he could not read very well and attended a general hospital for glasses. He was then told that there was something wrong with the right eye and that glasses would not help (no record from Hospital traceable). He only became conscious of something wrong about one year ago: "there was a film over the eye occasionally, and this seemed to disappear when he rubbed his eye". The eye was never red or painful. About 6 months ago the sight got worse as he could only see on the outer side.

Family History: nothing to record.

On examination: R. tension raised 65 mm. McLean fundus not seen - perception bad - eye trans-illuminated evenly.

Left eye: V = 6/5. Fundus normal. Full field (visual) - Tension = 25 McLean.

The right eye was removed on 23. 6. 1931. There was a small greyish-brown tumour the size of a hazel nut occupying post. pole of the eye and covering O.D.

PLATE VII.

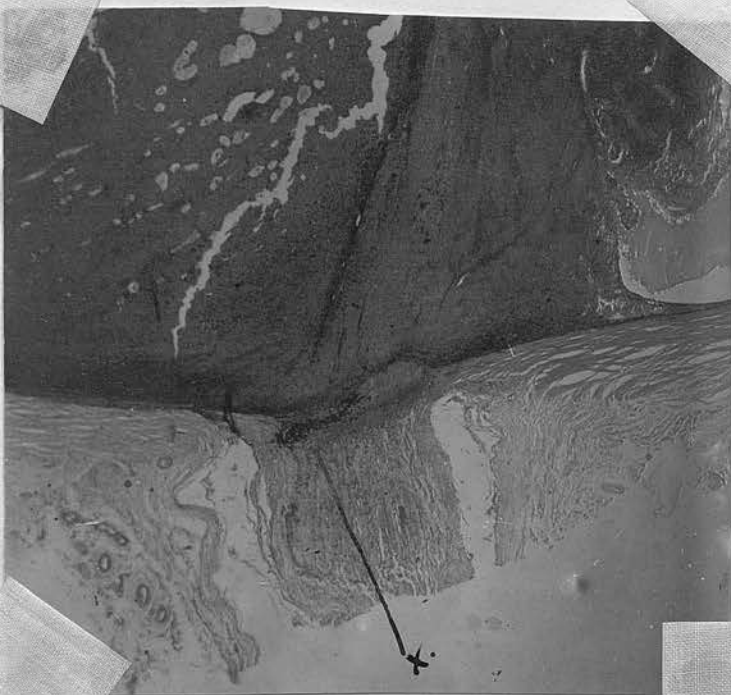


Fig. I. Section through optic nerve showing tumour invasion. (Case. I5). (X.)

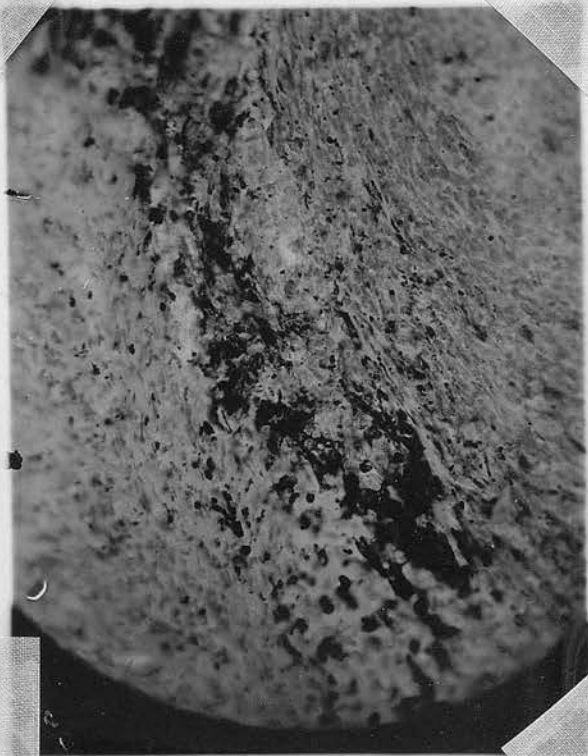


Fig. 2. Section shows deeply packed cells of the polihedral type mostly (Case I5).

No extra-ocular extension noted. The cells were closely packed and with very little tendency to spindle shape - more of polyhedral type, with very little stroma and simulating cancer formation - no whorling - cytoplasm scanty - nuclei large, variable and vesicular. Some mitosis - pigment moderate - vessels numerous and badly formed. Haemorrhage into tumour.

This patient was seen in September 1931. Felt well after operation but has had trouble with his stomach. He went to a hospital and was told he had a gastric ulcer. The liver is distinctly enlarged and with some tenderness. No fluid in abdomen.

Blood: No melanin. Lymphocytes 33%; Eosinophils 2%; Large Mononuclears 3%; Polymorphs 62%. No abnormal cells.

Urine: No melanin.

X-ray chest, etc: Calcified root glands: Nil in liver, but this was enlarged.

Case XVI. George P--, 62 years, was seen in January, 1929. He gave a history of a fall into a hole in the road in November 1928. There was a detachment of the retina on the right side, and which gave a dull shadow on trans-illumination. About two weeks ago he

developed acute glaucoma (May 1929). Vision = No P. of L. Eye painful. The right eye was enucleated. There was a small pigmented mushroom-shaped tumour growing between ora serrata and equator. No extra-ocular extension. The cells are polyhedral in type, and in parts definite spindle shaped. A good deal of cytoplasm - vesicular nuclei with marked nucleolus. Most of the cells had fine pigment granules. Fairly vascular and vessels badly formed. Some mitosis and haemorrhages.

This patient was not seen in September 1931, in spite of several letters to him. I am told he is still alive and well.

Case XVII. Vincent S--, 36 years old, was seen in November 1929. Has spent several years abroad, and was seen by several oculists.

Previous History: Dysentery - bad teeth.

He complained of difficulty with his sight and when examined by one oculist, the diagnosis was Cysticercus of retina. The trans-illumination was clear. There was a detachment of retina on inner side of globe, with corresponding loss of visual field. Small hazy haemorrhage over the detachment. Tension not raised. No eosinophilia present.

PLATE VIII.

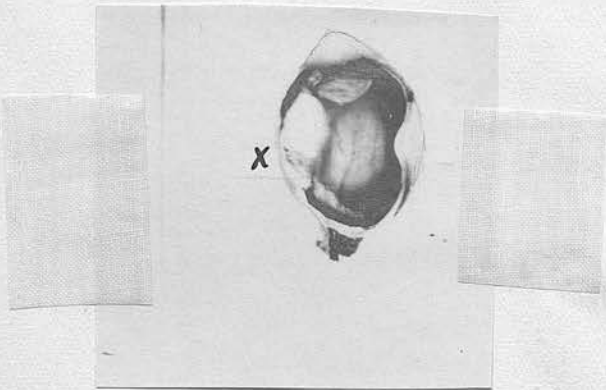


Fig. I. Section through tumour showing a pigmented band. (x). (Case I7.)

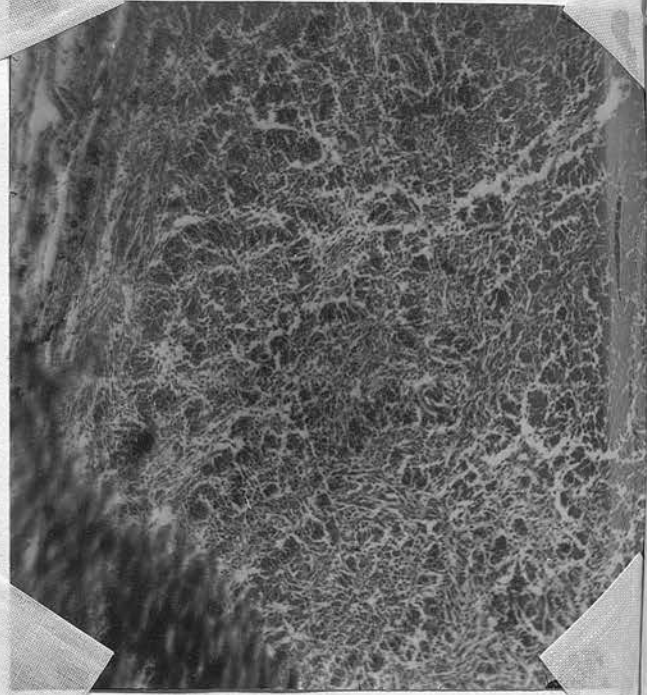


Fig. 2. Section showing spindle cells and beside these cells of carcinomatous appearance. (Case I7.)

The right eye was removed in November 1929. There was a tumour 15 x 6 mm. from ciliary region to posterior 1/3rd of globe - a whitish tumour, but dark pigmentary band through it. No signs of extra-ocular extension.

Tumour cells are mostly of the spindle type with fairly large nuclei. A fair amount of pigmentation evenly distributed throughout the tumour. In other parts cells are polyhedral, in type - not much mitosis. Vessels were poorly developed. No extra-ocular extension seen.

Patient is still alive and well.

Case XVIII. T. K--, 50 years, came up on 9th October 1930 for glasses. He has had frequent colds and consulted several oculists. There was pus in left antrum. R.V. = 6/5, L.V. = 6/6 - a defect in his visual field was detected by his attitude in looking at the test types. Eye from external appearances looked perfectly normal. A detachment of retina was discovered below with no movements - rather brownish. He was put to bed, and the detachment seemed rather less and was less hazy, - no floating opacities. He was seen again on 15th November 1930 - the vision was reduced to 6/18. There was slight lental opacity.

The left eye was removed in November 1930. The tumour was definite spindle in type, showing marked whorling. Cell nuclei large and often vesicular, with distinct nucleoli - moderately vascular. Vessels fairly well formed - pigment scanty - some mitosis - inner layers of sclera infiltrated. Type of tumour similar to Case X.

In September 1931 patient is alive and well - no enlargement of liver.

Case XIX. Mrs. Annie M--, aged 70, housewife, came up on 12th September, 1931, complaining of defective sight, and a black speck in the white of the eye. She noticed bright lights since winter of 1930.

Family History: Nothing to record.

On examination. The iris was pushed forwards about 40' clock, and a small black speck below it shining through sclera in ciliary region - good fundus reflex - no detachment seen. R.V. \bar{c} glasses = 6/12. Tension normal. L.V. = 6/36. Tension normal. The left eye was removed on 16th September, 1931.

Urine: no melanin.

Blood: No melanin and no abnormal cells.

Chest and abdomen: Nothing abnormal discovered.

X-ray Chest etc. There is an apparent nodule in upper left lung. Nothing abnormal on right side or in liver.

There was a flat pigmented tumour with unpigmented centre and about 14 mm. long by 4 mm. thick. It was just behind ora serrata and growing forwards to ciliary region. The cells were definitely spindle type, - some attempt at whorling. Pigmentation throughout. Vessels poorly formed, and there was a fair amount of mitosis. There is definite extension of tumour through to anterior layer of sclera and mostly around anterior ciliary vessels. The A.C. is compressed on this side, and there is adhesion of iris to cornea.

This patient is still alive and apparently fit.

Oct. 9. I have since been told that this patient's relatives were informed by a hospital physician that she was "riddled with cancer" in her body.

TRETTENERO (A)

Annal di Ottal, e clin. ocul. March 1931.

WHITNALL.

Anatomy of the Human Orbit.

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Charles William Yow.



21. XII. 31

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