Cerebellopontine angle tumours in black South Africans — how rare are acoustic schwannomas?

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Summary

Previous reports of intracranial neoplasms from Africa have all shown a very low incidence of acoustic schwannomas (neuromas). In this series a group of 11 cerebellopontine angle solid tumours from black Africans were studied. On conventional histological examination only 3 had the features of a schwannoma. However, by using immunohistochemistry, a further 3 examples were identified. As controls, the same antisera were also applied to known schwannomas and meningiomas. During the period of the study, 163 patients with primary intracranial neoplasms were seen and thus acoustic schwannomas accounted for 3,7%. Although this figure is low by world standards, it still represents a far higher figure than has previously been reported from Africa. This study therefore emphasises the value of immunohistochemistry in the diagnosis of brain tumours and, furthermore, shows that acoustic schwannoma must be considered in the appropriate clinical setting, even in a group previously regarded as low-risk.

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Studies from various parts of the world on the relative frequency of primary intracranial tumours have shown a marked variation in the proportion accounted for by acoustic schwannomas. This is highest in Asia, with figures of 10,2% from mainland China[1] and 10,6% from India.[2] Lower percentages were found in studies from the USA (4,0%),[3] Switzerland (8,9%)[4] and England (4,9%),[5] although in the last of these surveys there was considerable variation between neighbouring health districts in all of which there was a roughly similar ethnic composition. The incidence is lowest of all among black people in Africa, with figures of 0,9% from Nigeria[6] and 0,5% in what was then Rhodesia[7] (compared with 3,7% in whites in the same article). Percentages were somewhat higher in Kenya (2,6%)[8] and also in Egypt (9%), although the population in the latter is mainly Arab.[9] In South Africa the low relative incidence in blacks was confirmed in the last major study in the Transvaal by Froman and Lipschitz[10] in 1970. They found only 1 acoustic schwannoma among 122 primary intracranial tumours.

A recent study by one of us[11] showed a rather higher figure (5 out of 163; 3,1%). It was suspected that this may have been due to the use of new immunohistochemical markers, which became available for routine diagnostic work in the latter part of the survey. The relative proportion of schwannomas was therefore investigated in more detail by applying a panel of antisera to all the cerebellopontine angle tumours in the series, including some which had originally been diagnosed as meningiomas, in order to determine whether the number of acoustic schwannomas in black South Africans had previously been underestimated.

Materials and methods

Between 1979 and 1983 11 black patients presented to Baragwanath Hospital, Johannesburg, with solid tumours of the cerebellopontine angle, on which surgical biopsies were done during removal. Paraffin-embedded tissue, which had been processed by the usual methods, was available from all these cases. Sections were stained with haematoxylin and eosin, and then incubated with a range of commercially available antisera (Table I). Appropriate positive and negative controls were

TABLE I. IMMUNOHISTOCHEMICAL ANTISERA USED

Antiserum	Source	Specificity
CAM 5.2	**Becton-Dickinson**	**Cytokeratin (low MW keratin) (some epithelial cells)**
HMFG 1 and 2	**Unipath**	**Epithelial membrane antigen (glandular cells and mesothelium)**
Keratin	**DAKO**	**High MW keratin (48 000-60 000 kD) (squamous cells)**
CEA	**DAKO**	**Carcino-embryonic antigen (some epithelial cells)**
S100	**DAKO**	**S100 protein (Schwann cells, melanocytes, myo-epithelial cells, and a few other miscellaneous cell types)**
Vimentin	**DAKO**	**Vimentin intermediate filament (connective tissue)**
GFAP	**DAKO**	**Glial fibrillary acidic protein (astrocytes)**
Desmin	**DAKO**	**Desmin intermediate filament (muscle)**
Factor VIII-related antigen	**Hoechst**	**Endothelial cells**
***Ulex europaeus* lectin**	**Leclab**	**Endothelial cells**

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TABLE II. CONTROLS — IMMUNOHISTOCHEMICAL PROFILE OF MENINGIOMAS AND SCHWANNOMAS

Tumour	Case	Sex	Age (yrs)	Site	Histology: Subtype	Histology: Psammoma bodies	Antisera: CAM 5.2	HMFG	Keratin	CEA	S100	Vimentin	GFAP	Desmin	Factor VIII*	*Ulex* * lectin
Meningioma	1	F	58	Parafalx	Psammomatous	++	0	D+	0	0	F+	D++	0	0	F+	F+
	2	M	75	Parietal convexity	Fibroblastic	0	0	D+	0	0	D+	D+	0	0	0	0
	3	F	74	Sylvian fissure	Meningothelial	+	0	D++	0	0	F±	D+++	0	0	0	0
	4	F	68	Parietal convexity	Psammomatous	+++	0	D++	0	0	F+	D+++	0	0	D+	D+
	5	M	62	Parafalx	Fibroblastic	+	0	D+	0	0	F+	D+++	0	0	0	0
	6	M	77	Parafalx	Meningothelial	+	0	D+	0	0	0	D++	0	0	0	0
	7	F	82	Lateral posterior cranial fossa (sigmoid sinus region)	Fibroblastic	+	0	F+	0	0	F+	D++	0	0	0	0
	8	M	74	Sylvian fissure	Meningothelial	0	0	D++	0	0	0	D++	0	0	0	0
	9	F	66	Parafalx	Psammomatous	+++	0	D++	F+	0	F+	D+++	F+	0	0	D+
	10	F	77	Inferior surface temporal lobe (middle fossa)	Meningothelial	+	0	D++	0	0	F±	D+++	0	0	0	0

Tumour	Case	Sex	Age (yrs)	Site	Histology: Verocay bodies	Histology: Vascular hyalinisation	Antisera: CAM 5.2	HMFG	Keratin	CEA	S100	Vimentin	GFAP	Desmin	Factor VIII*	*Ulex* * lectin
Schwannoma	1	M	35	Ankle	+++	+	0	0	F±	0	D+++	D++	0	0	0	F+
	2	M	37	Face	+++	0	0	0	0	0	D++	D++	0	0	0	D+
	3	F	61	Lower leg	+++	+	0	0	0	0	D+++	D+	0	0	D+	0
	4	M	53	Finger	+++	+	0	0	0	0	D+++	D+	0	0	0	D+
	5	F	43	Neck	+++	++	0	0	F±	0	D++	D++	0	0	0	0
	6	F	67	Internal auditory meatus	++	0	0	0	0	0	D++	F+	0	0	F+	F+

*In all cases endothelial cells of blood vessels reacted positively with factor VIII-related antigen and *Ulex europaeus* lectin.
D = diffuse staining; F = focal staining; 0 = negative staining; ± = equivocal or marginally positive staining; ++ = strongly positive staining.

TABLE III. CEREBELLOPONTINE ANGLE TUMOURS

Group	Case	Sex	Age (yrs)	Site	Histological diagnosis	Selected histological features: Verocay bodies	Perivascular hyalinisation	Whorls	Psammoma bodies	Antisera: CAM	HMFG	S100	Vimentin
A	1	F	51	R CPA, Meckel's cave	Haemangiopericytic meningioma	0	0	0	0	0	F+	0	D+++
	2	M	24	L CPA, undersurface of tent	Meningothelial meningioma	0	++	+	+	0	F+	0	D++
	3	M	54	L CPA, clivus	Meningothelial meningioma	0	0	++	0*	0	F+	0	D++
	4	F	50	R CPA	Meningothelial meningioma	0	+	+	+	0	F±	F+	D++
	5	M	42	L CPA, clivus	Meningothelial meningioma	0	0	+	0	0	D++	0	D+++
B	6	M	40	L CPA	Schwannoma	+	+	0	0	0	0	D+++	D+
	7	F	25	L CPA into cerebellar hemisphere	Schwannoma	++	0	0	0	0	0	D++	D++
	8	F	58	L CPA	Schwannoma	++	++	0	0	0	0	D++	D++
C	9	F	45	R CPA to sigmoid sinus region	Spindle cell tumour	0	+	0	0	0	0	D++	F±
	10	F	43	R CPA	Spindle cell tumour	0	0	0	0*	0	0	D++	D+++
	11	M	59	R CPA, undersurface of tent	Spindle cell tumour	0	+	+	0*	0	0	D+++	D+++

*Focal calcification, but not true psammoma bodies.
D = diffuse staining; F = focal staining; 0 = negative staining; ± = equivocal or marginally positive staining; ++ = strongly positive staining; CPA = cerebellopontine angle.

employed. The same (and also some additional) markers were applied to sections from 10 mainly supratentorial meningiomas discovered incidentally at autopsy in Exeter, to 5 peripheral schwannomas from the surgical pathology archives, and to an acoustic schwannoma discovered incidentally at autopsy (Table II).

Results

The results from the control group of meningiomas are summarised in Table II. All showed diffuse reactivity with Vimentin, and all stained positively with HMFG, in all but 1 case diffusely. Six out of 10 were positive with S100, but in only 1 case diffusely. Tumours with plentiful psammoma bodies reacted to some degree with most antisera, this perhaps being due to artefact, since sections were more difficult to cut and prepare. Table II also summarises the results from the control schwannomas. All reacted moderately or very strongly with S100 and to a lesser extent with Vimentin, but all were negative with HMFG. Therefore, in order to discriminate between the two neoplasms, a strong reaction with S100 favoured schwannoma, while HMFG staining indicated a meningioma. Table III summarises the histopathological and immunohistochemical findings in the study group of cerebellopontine angle tumours. They are subdivided into groups indicating a firm diagnosis on histological grounds of meningioma (A) (Fig. 1), or schwannoma (B) (Fig. 2), and thirdly, those neoplasms in which typical features of these tumours were either lacking (Fig. 3) or present but contradictory (C). Each of this last group was originally labelled as meningioma by experienced general histopathologists. Some of the histological features of each tumour are listed to illustrate how a diagnosis was reached in cases from groups A and B, and the difficulties in group C.

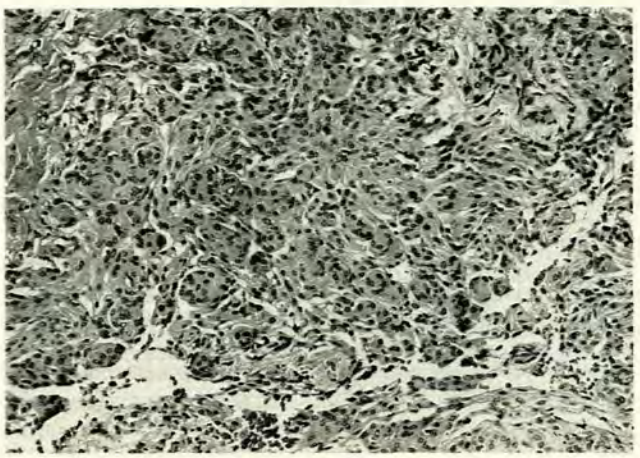

Fig. 1. Micrograph of case 3 showing unmistakable features of a meningioma with well-marked whorl formation (H and E × 160).

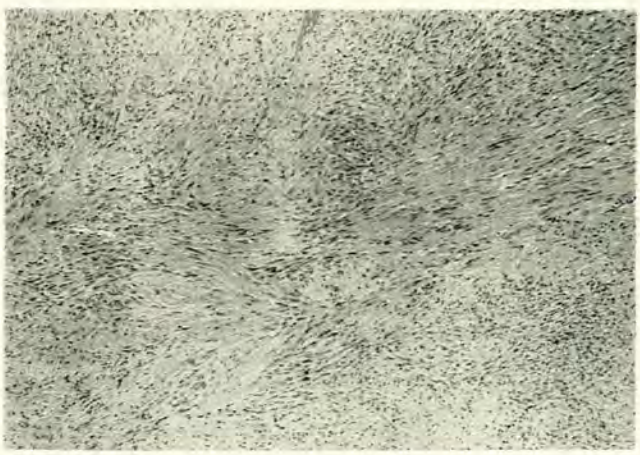

Fig. 2. Micrograph of case 7 showing nuclear palisading characteristic of a schwannoma (H and E × 100).

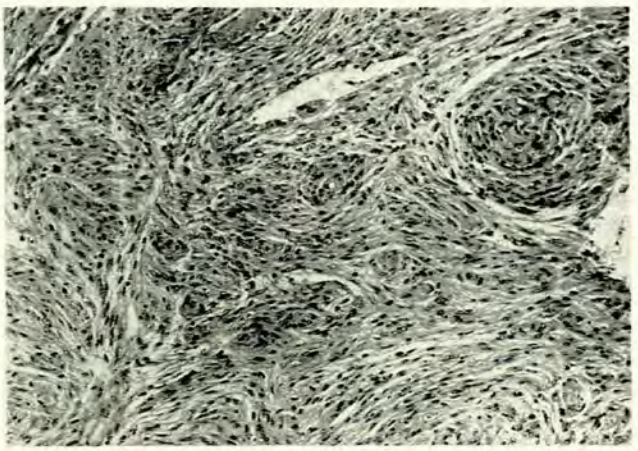

Fig. 3. Micrograph of case 11 showing a spindle cell tumour with some whorl formation (H and E × 160).

Immunohistochemical reactivity in group A was the same as the control meningiomas in Table II except for case 4, in which the staining for HMFG was equivocal at most. Similarly, the reactions of the tumours in group B were the same as for the control schwannomas. In the 3 cases in group C the staining pattern was that of schwannomas and not meningiomas (Fig. 4).

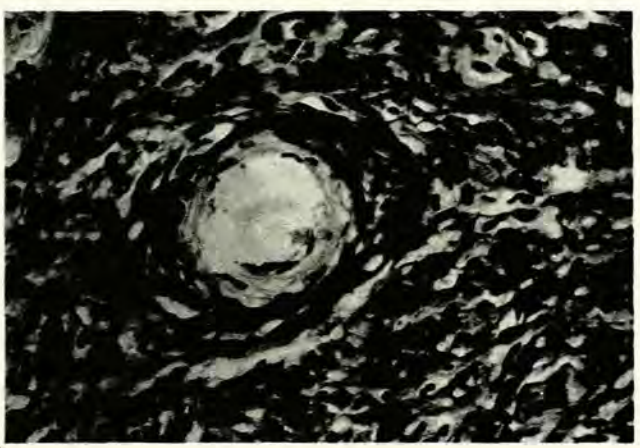

Fig. 4. Micrograph of case 11 with dark cytoplasm indicating a strongly positive reaction (S100 protein × 400).

Discussion

It is not always possible to differentiate acoustic schwannomas from cerebellopontine angle meningiomas either clinically or at operation. This is particularly the case if the tumour is closely associated with, or adherent to, both the meninges and the VIIIth cranial nerve. Microscopic examination of haematoxylin and eosin-stained sections is often sufficient to make the distinction but not always, particularly with the fibroblastic subtype of meningioma. In many cases, diagnostic features of

one or the other neoplasm are lacking in the tissue available for study, and the lesion can only be described as a spindle cell tumour. In the present series nearly one-third of the cases fell in this group. Furthermore, the differences on histological examination between the two entities are not always clear-cut, since meningioma-like whorls are sometimes seen in schwannomas,[12] and Verocay bodies have been described in meningiomas[13] (also personal observations).

This diagnostic problem can largely be solved by use of either electron microscopy or immunohistochemistry. The two tumours have different ultrastructural features that should lead to correct identification in almost every case,[14] but electron microscopy is not always readily available. Immunohistochemistry is a satisfactory alternative in this situation, where the reaction profile will also lead to a correct diagnosis in nearly every instance. It can be seen from the controls in the present study (Table II) that the most useful markers are HMFG (epithelial membrane antigen), which is positive in meningiomas and not schwannomas, and S100, which, conversely, is strongly positive in the latter and reacts only weakly, or not at all, with the former. These findings are in accordance with previously published series of meningiomas[15] and schwannomas.[16] It is worth emphasising that the markers used in this study are all commercially available. HMFG reacts with epithelial membrane antigen, and stains a wide variety of epithelial cells as well as mesothelium. S100 is a cytoplasmic protein, and stains several cell types; in general histopathological practice, its main uses are for identifying myo-epithelial cells, and also malignant (especially amelanotic) melanomas and tumours of nerve sheath origin.

A third method for differentiating between these two neoplasms involves cell culture. In another series one of us (M.S.D.) has shown that all meningiomas grew well after 3 days whereas the schwannomas failed to grow at all (unpublished observations). However, this technique is not readily available in routine surgical neuropathology practice.

Therefore in the present series we were able to identify 6 cerebellopontine angle tumours as schwannomas, which is double the number had only conventional histological techniques been used. Consequently, schwannomas accounted for 3,7% of the primary intracranial neoplasms in the complete series of 163.[11] This is higher than any previously reported figure among black Africans, and indeed is almost comparable to percentages from Europe and North America. We feel this high figure merely reflects better diagnostic techniques, although it is possible that it could indicate a genuine increase in incidence since the last major study of the same population in 1970.[10] We therefore conclude that acoustic schwannoma is not a rarity in Africa, and is a diagnosis that must be considered in the appropriate clinical setting.

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