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Expert Commentary on "Some Observations on Intracranial Glioma" by Ramesh Chandra, Sanatan Rath, K V. Mathai and Jacob Chandy

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Full Text

I deem it a privilege to be asked by the Editor, Neurology India to write a commentary on this iconic paper contributed by the founder of Indian Neurosurgery and his students a little over half a century ago. Going through this paper brought nostalgic memories of the trials and the tribulations of neurosurgery of that era which we shared with these pioneers. In addition, the subject continued to be of personal interest to us at the All India Institute of Medical Sciences.

This paper was undoubtedly the first detailed analysis of a large series of gliomas reported from India. This was based on a consecutive series of such cases treated at the Christian Medical College, Vellore between January 1950 and March 1960 in the very first formal neurosurgical services in India. The paper deals with a retrospective study of 482 cases of intracranial gliomas. In the same volume of Neurology India, Rath, Mathai and Chandy reported a series of 1711 cases of Intracranial space-occupying lesions (ICSOL) of which were historically verified, while the diagnosis was clinically based on 219.

The detailed information provided on these patients testifies the scientific rigour inculcated by Prof. Chandy from the very inception of his service. A decade later, Mathai revisited the subject of ICSOL as a review of 2332 cases[1] (Mathai 1978).

It is worth noting that the 1967 volume of Neurology India contained another detailed paper on the subject based on 1000 intracranial space-occupying lesions by a pioneer neuropathologist of the country, Darab Dastur (Dastur 1967) from Bombay (Mumbai).[2]

Around the same time, H.M. Dastur and Anil Desai also from Bombay published a landmark paper in Brain comparing the clinical features of 107 cases each of brain tuberculomas and gliomas[3] (Dastur and Desai 1965). We at the All India Institute of Medical Sciences made our first contribution on the subject by publishing "A Five-year Survey of B Intracranial space-occupying lesions"[4] (Tandon et al. 1970). Around the

same time, some other papers on intracranial space-occupying lesions, including gliomas, from CMC itself Madras and Bombay[5],[6],[7] (Abraham et al. 1964; Balasubramaniam and Ramamurthi 1964; Dastur and Iyer 1966).

It is not surprising that most of the patients arrived at the late stage of the disease. Thus, 83% of the cases had changes in fundus. It is worth noting that prior to the definitive surgery, 36% of the supratentorial, 23% of the infratentorial and 31% of the other gliomas had one or more clinical episodes of neural compromise, indicating tentorial or foraminal herniation. Bilateral papilloedema was present in 67%, 13% had secondary optic atrophy and 3% had primary optic atrophy. Thus, visual deficits were observed in nearly two-thirds of the patients; almost a third had a motor deficit. The advanced stage of the disease is reflected in the abnormalities (evidence of raised intracranial pressure) observed in nearly 80% of the plain X-rays.

For diagnosis of these tumours, one relied on old imaging techniques: pneumoencephalography, ventriculography and angiography. The authors have detailed post-operative mortality in all honesty. This was "33.1%, 37% and 30.8% respectively in supratentorial, infratentorial and third ventricular brain stem and optic glioma groups".

Before the current generation of young neurosurgeons pass a hasty adverse comment on the high surgical mortality mentioned here, it is important to refer to the international status around this time. Large series of cases reported from all over the world illustrate a similar very high immediate post-operative mortality of 20 to 40%.[8],[9],[10],[11],[12],[13],[14],[15] (Grant 1956, Elvidge & Martinez -con (1956) Levy & Elvidege (1956), Tonnis and Walter 1959, Ley et al. 1962, Jelsema and Bury 1967, Kunicki et al. 1969, Elvidge 1970.

Let me remind the readers that the series included the patients from January 1950, at a time when even CMC Vellore did not have the current basic minimal facilities for neurosurgery. I take the liberty to quote some extracts from the autobiography of Dr Chandy, "Reminiscences and Reflections". His thoughts on initiating neurosurgery at that time. "There was no one to help me, no one to guide me. There was no one to tell me what was expected of me. The very thought of speciality work in Neurology and Neurosurgery in India was not accepted anywhere at that time and no physician or surgeon could comment on it"[16] (Chandy 1988 pg 53). And, further on, "I had felt several times in my career that He, the Great Physician, was directly guiding me in making a specific decision about the operations. Such confidence and belief had helped me throughout my life" CMC Vellore which at that time was considered to be one of better-equipped hospitals, had regular anaesthesia department only one year before Dr Chandy initiated neurosurgery. A blood bank was established just around that time (Chandy 1988).

This reminds me that similar circumstances and feelings were shared by all those who initiated neurosurgery in the country around that time.* A personal anecdote, in this regard, is included here. In 1964, three years after initiating Neurosurgery at my alma mater, K.G. Medical College, Lucknow, my mentor, Prof. Kristian Kristiansen, visited us experiencing first hand the working facilities we had. He soon after his return in a talk at MNI commented, "If I had not seen his patients alive with my own eyes, I would not have believed that surgery was possible with such limited facilities".

In this connection, it is important to quote from the paper under review; "Post-operative mortality was high during the period prior to 1961. The use of anti edema measures such as urea, steroids and CSF by-pass methods had been routine measure since then. These helped in the reduction of immediate mortality rate. The immediate mortality rate for the whole period under review was 33.8%. The mortality rate after 1961 was only 22.5%." Introduction of dexamethasone in the pre and post-operative period, first recommended by Galicich in 1961, proved to be a distinct landmark in reducing the operative mortality dramatically[17] (Galicich, French & Melby 1961). This was nearly as good as those reported from abroad.

I take this opportunity to mention our own experience of AIIMS regarding reducing post-operative mortality over the years. Before 1970 (Tandon et al. 1970), this had already come down below to 20%. However, among 500 consecutive cases of supratentorial gliomas- both of dominant and non-dominant hemispheres, operated upon between 1973-1983.[18] The postoperative mortality was 13.96% and 14.34%, respectively (Tandon et al. 1986). This further reduced to 8.4% of 639 supratentorial gliomas operated upon between 1982-1989[19] (Tandon 1994). On my request, Prof Chandra has provided the latest figures from the Department. Between 2015-19, a total of 1400 gliomas were operated upon. Four hundred among these underwent emergency surgery owing to the poor clinical conditions. The mortality rate for the planned

surgery was less than one per cent, while those operated in an emergency; it was 4%. I have no doubt that this would be so in most neurosurgical departments in the country today.

It is interesting to note that the authors of the paper under review had found the gross total excision of the tumour to be ideal. This itself might be responsible for lower mortality since most reported series had indicated tumour biopsy to carry higher mortality. Surprisingly, the debate regarding biopsy followed by radiotherapy remained a therapeutic choice in many centres abroad especially in the UK at least till 1980.

Not only was radical/ gross total excision of these tumours was adopted as a policy, but it also appears that the centre did not exclude surgery on dominant hemispheres. The authors state that the "subtotal excision and decompression was the method of choice when the neurological function had to be preserved". Many centres abroad considered surgery on dominant hemisphere gliomas to be a contraindication (Pastzor 1980).[20]

A very important feature of the paper under review is the detailed information provided about follow-up which was available for 69%. Considering that their patients had come from all parts of the country, this is a creditable achievement. The detailed information provided on surgical outcome and follow up status can serve for comparison whenever new or different therapeutic strategies are introduced. In addition, the authors have provided valuable information on the quality of survival for various pathological types of gliomas. At the time when this paper was published, most neurosurgeons were concerned with saving life (reducing mortality) and prolonging life (duration of survival). However, now when the post-operative mortality has virtually come down to below two per cent and all efforts to prolong the duration of survival have only resulted in minor gains, only recently attention is being paid to the health-related quality of life (Ammirati et al. 1987, Brown et al. 2005).[21],[22]

However, we at AIIMS did not differentiate in our surgical approach to such tumours since we found that radical surgical decompression can be safely carried out without exacerbating the neurological deficit and even improving the existing deficit in a significant proportion of patients (Tandon et al. 1986, Tandon, Mahapatra and Khosla 1993). This was acknowledged by Garfield (1987) in the Northfield's surgery of the Nervous System. It is worth pointing out that this was prior to the availability of FMRI functional localization, or the more recent technological tools for surgery.[23],[24]

Interestingly there is a recent interest in this respect among neurosurgeons in the country. Arivazhagan (2019) has highlighted this in his paper, "Shifting goalposts and paradigm shifts: Trends in outcome evaluation in Glioma Management. A paper by Khatri et al. (2019) discusses "Health-related Quality of Life after Surgery in Supratentorial Glioma". This goes to show how advanced the authors of the paper were in their thinking on the subject, not restricted to "Chest-Beating" surgical success so common among most neurosurgeons. From the time the paper under review was published, phenomenal advances have been made with respect to tumour biology, diagnostic case and precision (CT, MRI, fMRI, Proton MRS) surgical techniques and technologies; the improvement in neuroanesthesia and intensive care facilities. Since that time, new techniques like availability of bipolar cautery, ultra-sonic aspirators, the introduction of micro neurosurgery, MRI, ultrasonic and fluorescence-guided surgery and more recently, robotic surgery have revolutionised neurosurgery.[25],[26] Similarly, there have been advances in radiotherapy, chemotherapy and the possibility of immunotherapy and gene therapy. At the same time, investigations based on molecular biology, genomics and proteomics, cytokinetic and labelling index have provided new insights already clinically utilised (Zlokovic, Michael, Apuzzo 1997; Klekner A et al. 2019, Stupp et al. 2009, Black 1999, Mineta et al. 1995, Glick et al. 1999, Mattie et al. 2005, Wildner 1999).[27],[28],[29],[30],[31],[32],[33],[34],[35],[36] Fortunately, Indian neuroscientists have kept pace with all these advances as it is evident from some of the references included here (Suri et al. 2011, Santosh et al. 2009, Sarkar et al. 2018, Sharma et al. 1985, Moiyadi 2016, Moiyadi and Stummer 2015).[37],[38],[39],[40],[41],[42]

While definite improvement has taken place in our understanding and better management of brain tumours including gliomas, it must be realised that we are still a long way from a cure. Operative mortality and morbidity has no doubt has improved, tumours that were considered inoperable at that time are now amenable to surgery. Long-term survival of selected ependymomas and medulloblastoma has been achieved. Let me quote Black (1999, "Corticosteroids, safer neuroanaesthesia, improved ICU care must take credit for this fall in mortality. CT, MR, Operating microscope, neuronavigation, functional localisation. While these developments contributed to mitigating the morbidity, they have done little to improve the ultimate prognosis

of the scourge that is glioblastoma".[31] Let me add the most other surgical techniques like MR, ultrasound and fluorescent guided surgery, has to be the best of my knowledge not made real improvements in the outcome[19] (Tandon 1994).

I have taken the liberty of quoting the papers illustrating some of the advances that have taken place since the paper under review was published, to highlight that these developments had not taken place at that time. Yet this does not reduce the scientific value of this paper. It sets a standard for a rapidly increasing number of neurosurgical services in the country, illustrating the scientific rigor to be pursued in precise recording and insightfully analysing one's experience for advancing knowledge and learning lessons for further improvement. I am happy to record that the seeds sown by Dr Chandy and other pioneers of Indian Neuroscience have blossomed today. The Editor of Neurology India, on my request, provided very heartening information that during the last ten years, there were 133 articles published on gliomas in other journals mostly by Indian authors, serves as its testimony.

Annexure

[SUPPORTING:1]

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