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RESEARCH ARTICLE

GAMMA KNIFE RADIOSURGERY IN PITUITARY TUMORS

Jitendra Bhadoria, Maneet Gill, Chinmaya Srivastava, Darpan Gupta, Lokesh Gautam and Sudhanshu Aggrawal

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Abstract

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Introduction:-

Pituitary adenomas are very common lesions, constituting between 10 and 20% of all primary brain tumors(1,2). Epidemiological studies have demonstrated that nearly 20% of the general population has a pituitary adenoma(2). Pituitary adenomas are broadly classified into two groups. The first category consists of tumors that secrete excess amounts of normal pituitary hormones, The second category of pituitary adenomas is composed of tumors that do not secrete any known biologically active pituitary hormones For both types of pituitary adenomas, a recurrence resulting from tumor invasion into surrounding structures or in complete tumor resection is quite common. Long-term tumor control rates after microsurgery alone vary from 50 to 80%(3-5). Radiation therapy or radiosurgery can be administered postoperatively as adjuvant therapy to inhibit recurrent growth or later when clinical symptoms or neuroimaging findings indicate a recurrence. These therapies may also be used postoperatively to treat known residual tumor following incomplete resection.

Conventional fractionated radiotherapy was initially designed to treat all kinds of cancers and subsequently, pituitary tumours were among the first brain tumours to be treated [6-8]. However, the dose that can be given is limited to 45-50 Gy with approximately 1.8 Gy given per day. This leads to a very slow reduction of elevated pituitary hormones. The broad field of radiation causes a high incidence of pituitary insufficiency [9,10]. Furthermore, major complications, although rare, involve damage to the optic pathways [11], necrosis in other brain areas and even neuropsychological complications [12]. In addition, the relative risk of the development of second brain tumour after fractionated radiotherapy is estimated to be significantly increased compared to the general population [13,14]. The limitations of radiotherapy have stimulated the interest to develop alternative methods to deliver radiation to pituitary tumours. Stereotactic radiosurgery allows the delivery of radiation with a high degree of precision to the target, and low doses to the surrounding tissues.

Gamma knife radiosurgery:-

In 1968 Lars Leksell carried out the first gamma thalamotomy in a patient with intractable cancer pain using the first stereotactic radiosurgical unit in Stockholm For the radiosurgical interventions the Leksell Stereotactic System is used. The procedure has recently been reviewed in detail. A special helmet allows irradiation with 201 gamma beams of ⁶⁰Co, and the irradiation is given as a single treatment lasting about 30 minutes. The treatment is carried out in an outpatient setting in local anesthesia and a stereotactic frame is attached to the skull. Before treatment, a stereotactic magnetic resonance imaging (MRI) with pre- and post-gadolinium axial and coronal views and three dimensional volume axial sequences is performed. Coronal images are also obtained by reformatting the axial scan information which reduces distortion. Dose planning requires delineation of the targets and the adjacent structures,

especially the optic chiasm. The gamma knife has four collimator sizes, 4, 8, 14 and 18 mm, through which ionizing radiation is delivered. In general the smaller the size of collimator used, the steeper the fall in radiation involving tissue outside the target. The dose plan frequently involves the use of multiple shots so as to deliver to the periphery of the tumour approximately 50% of the maximum dose of radiation administered (50% isodose line).

We present our series of 152 cases of pituitary tumors, treated with gamma knife radiosurgery over the last 10 years. This investigation was conducted to evaluate the effects of gamma knife radiosurgery on the growth and safety in the treatment of pituitary adenomas.

Material And Method:-

This retrospective study carried out at the apex tertiary care centre of the armed forces medical setup in India, retrospectively analysed the use of Gamma knife radiosurgery as a primary or adjunctive form of therapy for pituitary tumors offered to patients over a period of 10 years at this centre. The radiosurgery was carried out using a Leksell Gamma knife Elekta instruments, Stockholm, Sweden, model 4 C, installed in 2007. The gamma knife was planned with safety tolerance limit of dose to brain stem, cranial nerve not to exceed 12 Gy. The prescribed tumor margin dose was more than 13 Gy if possible. A retrospective chart analysis of 152 patients who underwent a radio surgical procedure as a primary or adjunctive therapy was carried out.

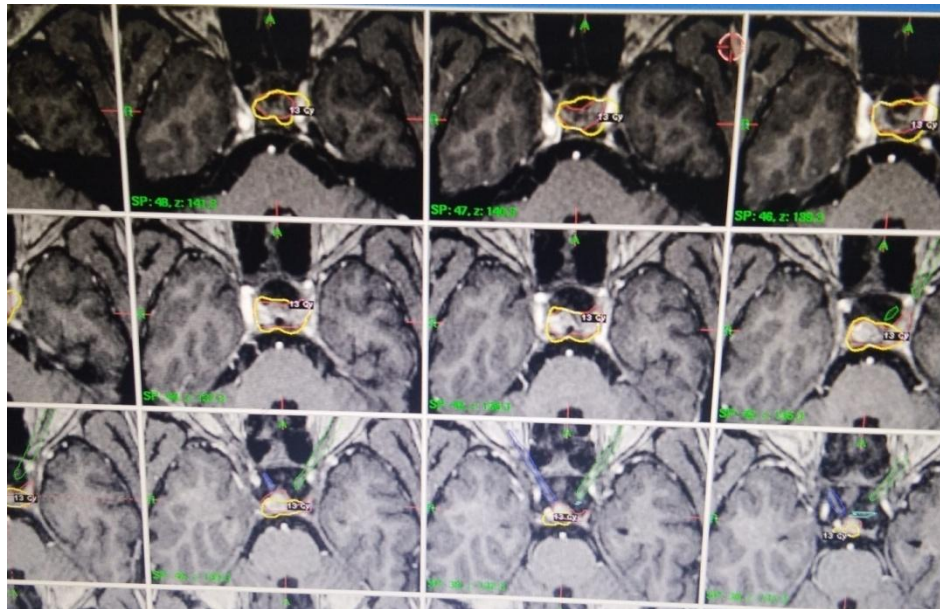


Fig1:- 32 years old female underwent gamma knife radiosurgery for residual pituitary adenoma. Dose of 13 Gy was given.

Age range	No
20-30	17
31-40	51
41-50	27
51-60	33
61-70	17
71-80	06
81-90	01

Mean age	Median age	Gender	Mean dose	Median dose	Mean volume
45.78	43.9	Male : 86	17.08 Gy	16 Gy	4.028 cc
		Female : 66			

Parameter	Mean	Median
Margin dose	15.53 Gy	15.5Gy

Max dose	30.72 Gy	31Gy
Isodose	50.5 Gy	50 Gy
Right optic nerve	8.73 Gy	8.45 Gy
Left optic nerve	7.60 Gy	7.9 Gy
Optic chiasma	7.84 Gy	7.75 Gy

Results:-

Of the 923 cases who received Gamma knife radiosurgery at this centre till Sep 2019, 152 cases with pituitary tumors underwent the procedure. 24 out of 152 cases received Gamma knife surgery as primary therapy. Out of these, 38 cases were of functional adenomas and 114 were non-functional. Male to female ratio was 1.3 :1. The average tumor volume was 4.02 CC and the average dose of radiation was 17.08 grey with the average tumor coverage being 94.59%. The follow-up has ranged from 6 months to 10 years.

There has been 8 patients lost to follow up. 22 out of 24 patients which received gamma knife radiosurgery primarily not only exhibited tumour control (defined as unchanged or reduced tumour volume in follow up) but also showed subtle improvement in status viz recovery of vision. The clinical improvement, if any, in cases where gamma knife surgery was offered as adjunctive postoperative therapy for residual lesion, was ignored to offset any confounding factor generated by spontaneous recovery over a period of time from iatrogenic neurological paresis caused by surgery. Four cases of tumor progression were noted in the present series, three of those patients underwent surgery and one patient was unwilling for surgery. Two patient had deterioration vision, but they also showed tumor progression.

Discussion:-

In the treatment of pituitary adenomas, radiotherapy is classically indicated in cases of incomplete resection or recurrent tumors, functioning tumors uncontrolled by medical therapy and patients inoperable or who refuse surgery.

The objectives of radiotherapy are the control of tumor growth and/or the normalization of hormonal secretion, the maintenance of pituitary function and preservation of neurological function, especially visual acuity. Prasad reported a control rate of tumor growth 67-100% with conventional radiotherapy [15]. Brada et al. reported tumor progression-free survival at 10 and 20 years of 94% and 89%, respectively [16]. Petrovich et al., also in a retrospective series of 78 patients treated only with the radiosurgery and a median prescribed dose of 15 Gy, reported a 96% tumor control, with volume reduction (> 50%) in 29% of cases after 36 months median follow-up [17]. Izawa et al., after mean follow up of 24 months in 79 patients, reported local tumor control in 93.6% of patients, with reduction in 24.1%. They prescribed a mean marginal dose of 22.5 Gy. The lower rate of tumor shrinkage in our series is probably related to a lower dose prescribed [18].

Conclusions:-

RS is an effective and safe therapeutic option in the management of selected patients with pituitary adenomas. The short latency of the radiation response, the highly acceptable radiological and hormonal control and absence of complications at this early follow-up are consistent with literature.

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