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Study On Surgical Treatment Of Intradural Extra medullary Spinal **Cord Tumors**

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Abstract

KEYWORDS In this study, we report the synthesis of novel Schiff bases and β -lactam derivatives derived from Astrocytoma, thiomorpholine and morpholine compounds, elucidating their antimicrobial, antioxidant, intramedullary, antituberculosis, anti-urease, and acetylcholinesterase inhibition properties. Our systematic extradural spinal cord investigation aimed at introducing innovative structures to the scientific literature, thereby tumour, subarachnoid contributing valuable insights to the field of medicinal chemistry. The synthesized compounds space, Medullary were rigorously screened for their biological activities, revealing noteworthy efficacy in various Cavity, Spinal Cord. domains. Compound 3b exhibited remarkable antituberculosis activity, while compounds 6a demonstrated potent Acetylcholinesterase Inhibition effects. Additionally, compound 3b displayed notable antioxidant capacity against standard drugs, underlining its potential therapeutic relevance. Moreover, compounds 3b, 6a, and 6b emerged as promising entities with excellent anti-urease activity against thiourea. Our study presents a significant advancement in the synthesis of structurally diverse compounds with morpholine and thiomorpholine moieties. The comprehensive screening of these compounds for diverse biological activities provides a nuanced understanding of their potential applications in medicinal chemistry. These findings contribute to the development of novel compounds with promising biological activities, fostering

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further exploration in drug discovery and development realms.

Introduction:

Spinal cord tumours are thought to account for 15% of all malignancies that impact the central nervous system [1,2]. The parenchymal cells of the spinal cord are the site of genesis for five to ten per cent of all cancer cases that develop there [1,2]. The remaining 90–95 per cent originate from cells near the spinal cord, such as spinal nerve roots or meningeal coverings. Unlike their cousins in the cranial area, primary spinal tumours are often not harmful. Spinal cord tumours surrounding the dura are categorized as extra- or intra-dural [2,3].

Regarding the dura, invasion is a less frequent underlying cause of clinical presentation than compression. Perinatal tumors can be classified as extramedullary or intramedullary based on where they are to the spinal cord. Intradural cancers account for three times as many cases as extradural ones [4]. While the frequency of intramedullary tumors is approximately thirty percent in adults, it can approach fifty percent in children [4].

Middle-aged people are the most likely to have a tumor of the spinal cord. Except for meningiomas, which are more common in females, the ratio of males to females is about the same. Meningiomas are more common in females. Following the cervical region in terms of severity was the region located in the cervical region [4]. The area of the lumbosacral region is affected only infrequently. Nerve sheath tumors usually appear at intradural extramedullary locations and account for thirty percent of the cases. More fabulous than twenty-five percent of all meningiomas are meningiomas [5]. Within the medullary cavity, astrocytomas and ependymomas are responsible for most of their proliferation [6]. Among the many types of tumors are hemangioblastomas, dermoids, epidermoids, lipomas, and secondary tumors. In addition to intramedullary locations, the conus medullaris is another possible location where the epidermis can appear [6,7]. Extramedullary and intramedullary components are present in pendymomas located in the conus and cauda equina areas, respectively [6].

The level and plane of the tumor can have an effect on the clinical signs and symptoms that are noticed in persons who have spinal cord tumors. These signs and symptoms can range from mild to severe. These traits help determine the clinical location of lesions [1,2]. This skillfully produced accurate clinical localization seldom coincides with radiological results, particularly those generated from the multiple MRI sequences that are now accessible. This is an unexpected finding. In addition, variations might be seen in both the intraoperative observations and the histopathological study [4]. Although they are referred to by a different name, benign intradural extramedullary (IDEM) tumors, which include those that spread beyond the dura, have traditionally posed a significant obstacle for neurosurgeons. In 1887, Sir Victor Horsley was the first person to successfully conduct a laminectomy resection on a spinal IDEM tumor [7]. The surgical methods that are used to treat these lesions have undergone continual development with time [8]. There is a wide range of neoplasms that include tumours that originate from the IDEM compartment of the spinal canal; however, the majority of these tumors do not exhibit any histological markers that are indicative of malignancy [9]. Surgery is typically the treatment option of choice for these tumors because of its capacity to give long-term management of cancer as well as long-term relief from the symptoms [1-7]. In light of this, the purpose of the current study was to explore the association between clinical and radiological presentation and histology, as well as the surgical treatment that was carried out and the results the surgery produced.

Materials & methods:

The research involved a total of thirty-six individuals who were diagnosed with spinal cord cancer and received treatment at the SCB Medical College in Cuttack during the months of December 2020 and May 2023. Everyone eligible to participate was enrolled in this prospective trial. A comprehensive collection of clinical, radiological, and pathological data about the 36 cases was recorded. Patients with spinal compressive myelopathy who were believed to have intradural extramedullary spinal cord tumors and patients with intradural extramedullary spinal cord tumors were candidates for participation in the research. The criteria for excluding participants from the study include spinal cord compression lesions brought on by disc problems. Lesions of the spinal cord that are caused by compression

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caused by traumatic injuries lesions of the spinal cord that are compressive and post-inflammatory in nature A comprehensive clinical examination that included the patient's medical history determined the motor, sensory, and reflex levels. To pinpoint the precise position of the tumour in the spinal cord, the highest level was utilized, and the vertebral level related to it was documented. To define the plane of the lesion, clinical criteria include loss of sensory function, loss of suspending sensory function with sacral sparing, loss of descending sensory function and motor weakness, and early involvement of the sphincter are all symptoms that are associated with intramedullary malignancies. Many symptoms can be related to intradural extramedullary malignancy, including radicular discomfort, loss of descending sensory function and motor weakness, and late involvement of the sphincter involvement. Some symptoms can be associated with extradural spinal cord tumours, including radicular discomfort, sensory loss or motor paralysis that develops with time, late sphincter involvement, and local spine soreness.

Clinical criteria to evaluate spinal cord tumours' pathophysiology include the following: Some of the hallmarks of schwannomas are the existence of root symptoms that are readily observable and the lesion plane located at the intradural-extramedullary level. All of the meningiomas included in the study were found to be most usually located in the thoracic cord and primarily affect females. The intradural extramedullary plane was the location where the tumor was discovered. Astrocytomas exhibited clinical manifestations that were comparable to those of ependymoma in paediatrics. The plane of the tumor was intramedullary, and the majority of the patients were younger. Among the extradural tumors of the spinal cord are dorsal tumors, which are responsible for symptoms such as chest tightness, bandlike paresthesia, and soreness in the spine.

To define the plane of the lesion, radiological criteria include the following: The creation of a syrinx is the consequence of intramedullary spinal cord tumours, which force the spinal cord to either grow or shrink more than it should. Myelographic and T2-weighted magnetic resonance imaging (MRI) pictures showed that the CSF gaps at the tumour level were getting smaller. On magnetic resonance imaging (MRI), extradural spinal cord malignancies manifested as cord compression and displacement, expansion of neighbouring spinal subarachnoid spaces, and a competing block that seemed to have a brush boundary from the outside. Intraduralextramedullary spinal cord tumours contributed to the development of the meniscus sign by causing the subarachnoid space on the side of the tumour to become more expansive, as well as by thickening the dura that was next to the tumour.

When determining sickness, radiographic criteria include positioning the tumor inside the medullary cavity, symmetry, persistent contrast enhancement, and an association with the syrinx that ranges from sixty-five to sixty-five percent. The astrocytoma was within the medullary cavity, had a weak border, and twenty percent of it was connected with the syrinx. The hemangioblastoma was distinguished bv its intramedullary location, significant contrast enhancement, and disproportionate syrinx. These characteristics were the differentiating characteristics. When seen by T2 imaging, Schwannomas are welldefined extramedullary tumours that exhibit iso- to hyper-intensity.

On the other hand, they seemed to have a more pleasing appearance. Neurofibromas can look like dumbbells since they are intradural extramedullary tumors with bone remodelling as a surrounding structure. Extramedullary tumors were seen within the dura mater of meningiomas, as well as hyperintense T2 pictures, isoto hypointense T1 images, intense contrast enhancement with calcification, and a dural tail. After completing a comprehensive clinical evaluation, each patient was subjected to a radiological examination, and all relevant information was documented. Surgical procedures were performed on the patients, and the removed tumour specimens were then sent for histological examination. Documentation about particular histological features has also been completed.

Statistical analysis:

After the data collection, Microsoft Excel 2010 and the Statistical Package for the Social Sciences (SPSS) were used to help with a comprehensive statistical analysis. Baseline statistics were used in the study, and the p-value was less than 0.05.

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JCHR (2023) 13(6), 2853-2861 | ISSN:2251-6727



Results:

Figure 1: Gender distribution in the study population



Figure 2: Comorbidities in the study population.



Figure 1 shows that out of the total of 36 patients who participated in the study, 22 (61.1%) were female and 14 (38.9%) were male. 37 out of 36 patients, or 97%, presented with weakness, measured by an MRC power grade of less than 4. A total of thirty patients, or 83%, did not have any comorbidities. Four patients, or 11%, had diabetes, and one patient, or 2.8%, had both hypothyroidism and asthma. Eleven of the thirty-six patients, or thirty-six per cent, presented with a loss of mobility or were bedridden based on their condition (Figure 2).

Figure 3: Tumor type (radiological) in the study population.



Meningioma and schwannoma were the most common radiological diagnoses among the entire research group, accounting for 14 (38.9%) of the total. Lipoma and dermoid followed in a distant second with two (5.6%) of the total, and finally, ependymoma, neurofibroma, enteric cyst, and arachnoid cyst each accounted for one (2.8%) of the total (Figure 3).

Figure 4: Histological diagnosis of tumours in the study population.



One patient with a radiological diagnosis of schwannoma left the hospital due to the COVID protocol. One patient with a radiological diagnosis of an enteric cyst was denied surgery after some clinical improvement and was discharged on request (Figure 4). Of the 36 patients, 34 patients decided to undergo surgery (either a hemilaminectomy or a laminectomy).

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JCHR (2023) 13(6), 2853-2861 | ISSN:2251-6727





Surgical procedures were performed on 34 of the 36 participants in the research. Meningiomas were found in 13 (36.1%) patients, while schwannoma was found in 11 (30.6%) patients with histopathological examinations. Additional diagnoses included lipoma in three cases (8.3%), dermoid in two cases (5.6%), ependymoma in two cases (5.6%), and astrocytoma, neurofibroma, and arachnoid cyst in one case (2.8%).

Out of the 36 patients who participated in the trial, 27 (75%) showed improvement, 6 (17.6%) stayed in the same condition as they were before surgery, and just one patient (2.8%) saw a decline after the procedure. Two individuals, or 5.6% of the total, have never had any surgical procedure.

The data of one post-operative patient were not included because the patient was lost to follow-up. Out of the 34 patients who underwent surgery, 31 (93.9%) had no recurrence, two (6.1%) had recurrence at follow-up, and the remaining post-operative patients had no recurrence. During the study, most patients (33,91.7%) showed up for follow-up, and just three patients (8.3%) were not found to be lost to follow-up. Seventeen of the thirty-four patients enrolled in the research and had surgery exhibited clinical improvement. In contrast, only thirtyseven per cent of the male patients showed improvement. According to the study's findings, out of the 33 patients who had surgery and presented with weakness, 26 (96.3%) exhibited clinical improvement after the procedure. Six patients stayed unchanged, and one patient experienced worsening. A single patient (3.7%) improved without any treatments being performed.

Nineteen of the twenty-four patients who underwent surgery and arrived with mobility (with or without help) exhibited improvement. In contrast, eight of the ten patients who did not have mobility showed improvement after surgery. The post-operative hospital stay for patients who underwent laminectomy was 7.05±1.5 days. In contrast, according to the study, the postoperative hospital stay for patients who underwent hemilaminectomy was 6.85±1.7 days, respectively. Seventeen of the thirty-four patients who underwent surgery are between forty and forty and older. On the other hand, out of the 17 patients who were under 40 years old, 13 (76.5%) exhibited clinical improvement. In contrast, in the group of patients who were over 40 years old, 14 (82.4%) showed improvement. 22 of the 36 patients that participated in the study were female, whereas 14 of the patients were male. Of the 22 female patients, 12 (54.5% of them) were over the age of 40, while 10 (45.5% of them) were under the age of 40. Similarly, out of the 14 male patients, eight (57.1% of them) were under the age of 40, and six (42.9% of them) were over the age of 40. The most common position in the group of individuals under 40 was thoracic (105.6%), followed by lumbar (3.7%). On the other hand, in the group of individuals over 40 years old, the most common location was thoracic (90.5%), followed by thoracolumbar (52.7%). When comparing the radiological diagnoses of individuals under 40, the most common diagnosis was schwannoma (9%), followed by meningioma (5%; 27.8%). On the other hand, in the group of individuals above 40, the most common diagnosis was meningioma (9%), followed by schwannoma (5%; 27.8%). Among patients under the age of 40, the most common histological diagnoses were meningioma (52.9%), schwannoma (529.4%), and meningioma (63.5%), according to the findings of the study. Thoracic (76.5%) > cervical (66.7%) > lumbar (50%) location came in second place in terms of clinical improvement following surgery. All of the research participants who belonged to the cervicothoracic and thoracolumbar locations showed improvement in their clinical condition compared to the lumbar location.

Discussion:

According to estimates, 40-45% of primary spine malignancies are caused by IDEM tumors [7–11]. Three people out of every 100,000 have these tumors. According to Nittner's calculations, the incidence of

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JCHR (2023) 13(6), 2853-2861 | ISSN:2251-6727



IDEM tumors in the general population is 0.3 per 100,000 individuals. According to a study [12], 22% of IDEM tumors occur in the cervical region, 22% in the lumbosacral level, and more than half are in the thoracic area. IDEM tumors most frequently occur in the thoracic region. The study found that, among participants aged 40 and above, the most common location was the thoracic (105.5%), followed by the lumbar (31.6%). The rates were similar. In contrast, the most common area among those over 40 was thoracic (90.5%), followed by thoraco-lumbar (52.7%).

The majority of IDEM tumors are found in females rather than males, and they often manifest themselves in the fourth to fifth decades of a person's life [13]. This is according to demographic observations. 79% It has been asserted that there is a significant feminine tendency, in particular with regard to meningioma. In a different research, the findings were found to be comparable, with 64.7% of the participants being female [14]. Narayan et al. performed a study, and the results showed that women outweighed males by a significant margin (54.3% against 45.75%, respectively) [15]. These findings are in line with the concept of IDEM tumor propensity, which is supported by the fact that the majority of patients were female. It is possible that this is connected to the action of estrogen; however, the mechanism that is responsible for this is unknown [16]. According to the findings of our current study, which were similar to those of previous investigations, 22 of the 36 patients were female, while 14 were male, which represents 61.1% and 38.9%, respectively. Twelve (54.5% of the 22 females) were older than forty years old, ten (45.5% of the men) were forty years old, eight (57.1% of the 14 males) was forty years old, and six (42.9% of the males) were forty years old.

The most common primary IDEM spinal tumor is schwannoma, which accounts for thirty to fifty percent of all cases, followed by meningioma, which accounts for twenty to twenty-five percent of all cases. In the Surveillance, Epidemiology, and End Results (SEER) database, which had 5564 cases in 2014, it was discovered that meningioma was the main intradural spinal tumor that occurred the most often. 30.7% of all instances were represented by this fact. It was discovered that 15.5% of the patients had Schwannomas as well as other types of nerve sheath cancers. The most prevalent radiological diagnoses in the research were meningioma and schwannoma, each of which affected 14 patients (38.9%). Lipoma and dermoid, each of which affected two patients (5.6%), followed by ependymoma, neurofibroma, enteric cyst, and arachnoid cyst, each of which affected one patient (2.8%) [17,18]. In the group of patients aged 40 years old, the most prevalent radiological diagnostic was schwannoma, which was found in 9 patients (50%) and was followed by meningioma, which was found in 5 patients (27.8%). Following the discovery of meningioma in 9 (50%) of those above the age of 40, schwannoma was discovered in 5 (27.8%) of those individuals.

Within the scope of the current investigation, 34 out of the 36 patients who had undergone surgical procedures had histological diagnoses that were in agreement with those that were provided by earlier research [19-22]. Meningiomas were found in thirteen (36.1%) of the subjects, while schwannomas were found in eleven (30.6%) of the people. Lipoma, which accounted for 3.8% of all cases, in addition to dermoid 2 (5.6%), ependymoma (2.6%), astrocytoma, neurofibroma, and arachnoid cysts (1.8%), were the subsequent most common types. Among the patients aged 40 and older, schwannoma was the most common histological diagnosis in six (35.3%) of them, followed by meningioma in four (23.5%) of them. On the other hand, among the patients aged over 40, meningioma was the most common histological diagnosis in nine (52.9%) of them, followed by schwannoma in five (29.4%) of them. These findings are in line with the findings of other studies [19-22].

According to the findings of the study [21], the most prevalent symptoms were soreness and numbness in the lower limbs, and these symptoms were detected in every single incident. The patients, seventy percent of them, had signs of motor weakness. Local or radicular pain, as well as sensory or motor weakening of the extremities, were found to be the most prevalent symptoms, according to a research [23]. Of the 36 people who were examined, 97 percent of them were found to be feeble, and 11 of them (30.6%) were found to have lost mobility. In the event that support structures, including as facets, capsules, and ligaments, are damaged during the process of laminectomy for the removal of a tumor, this have the potential to lead to spinal instability and deformity. It is for this reason that hemilaminectomy is an acceptable procedure for IDEM tumor excision [24-27]. A

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JCHR (2023) 13(6), 2853-2861 | ISSN:2251-6727



significant proportion of intraepithelial neoplasms (IDEM) are classified as meningiomas or nerve sheath tumors. The latter category encompasses both schwannomas and neurofibromas. In most cases, the objective of surgical procedures is to achieve total microscopic excision while simultaneously preserving and improving neurological function [24-21]. 6. Due to COVID guidelines, one patient with a radiological diagnostic of schwannoma was discharged from the hospital, while another patient with a radiological diagnosis of intestinal cyst declined surgery after experiencing some clinical improvement and was discharged on their own accord [23]. Laminectomy was performed on 58.3 percent of the 36 patients who participated in the research, whereas hemilaminectomy was performed on 13 patients (36.2%).

With an improved Frankel score at the conclusion of the follow-up period, the majority of persons (77.14%) had a satisfying result, according to the findings of a research study that followed up on them for a period of one year [15]. In a research that was published in 2022 by Meng and colleagues, it was discovered that there was a substantial difference between the JOA score and Nurick's grade in patients both before and after they had laminectomy [29]. In addition, Govind et al. discovered that the majority of individuals had great results following one-month and six-month post-operative follow-ups [28]. The percentages were 37.3% and 61.2%. respectively. Numerous studies have demonstrated that the neurological recovery following surgery is remarkable. In a study conducted by Konovalov and colleagues [29], it was demonstrated that fifty percent of patients advanced to a higher functional class on the McCormick scale following laminectomy and tumor removal. Only one patient (2.8%) had a decline in their condition after surgery, while the remaining six (17.6%) patients stayed at their preoperative level. Previous research indicates that 27 (75%) of the 36 patients who participated in this study showed improvement. Two of them, or 5.6%, had never been surgically operated on. Only seventeen of the thirtyfour patients who underwent surgery were between the ages of forty and forty years old. It is consistent with the findings of earlier trials that thirteen patients aged forty years showed clinical improvement, whereas fourteen patients aged forty years or older showed improvement. 13 of these patients (76.5%) demonstrated clinical

improvement. Thoracic (76.5%) locations performed better than cervical (66.7%) and lumbar (50%) locations after surgery. All patients (100%), including those with cervicothoracic and thoracolumbar sites, responded favorably to the procedure. Following surgical removal of neurofibromas, lipomas, astrocytomas, and arachnoid cysts, meningiomas (84.6% of cases) and schwannomas (72.7% of cases) showed signs of improvement.

A total of thirty patients, or eighty-three percent, had surgery without any comorbidities. Two patients, or eleven percent, were diagnosed with diabetes, and one patient, or two and a half percent, had both hypothyroidism and asthma. There was a 7.2% recurrence rate of spinal tumors that was identified, with IDEM masses returning more frequently than other types of tumors [21]. After five and fifteen years, respectively, ten percent and twenty-eight percent of the SNSTs that had been completely eliminated resurfaced. There are other instances, including neurofibromas and schwannomas, which include neuromas, neurinomas, and neurilemmomas. (94,95) Whenever there are malignancies that have not been removed and/or recurrences [30,31]. In accordance with the findings of El-Mahdy et al [32], the rate of post-operative recurrence for IDEM tumors is sixteen percent. As stated by Asazuma et al. [33], they noticed that 100 intraspinal neoplasms, which is 7.2% of the total, recurred. IDEM spinal tumors, which recurred more commonly than other intraspinal tumors, were found in 46% of those individuals under consideration [33]. This study, which was nearly equivalent to the data that was published in the literature, found that 31 (93.9%) of the 34 patients who underwent surgery did not have a recurrence of the disease. Two patients (6.1%) experienced a recurrence at the follow-up, and the data of one patient were not included because they were lost to follow-up.

Conclusion:

In order to effectively treat IDEM tumors that are situated in the spine, neurosurgeons need to be well prepared. As a result of the close proximity of these tumors to significant regions of the brain, it will be difficult to achieve this aim. In spite of the fact that the treatment of various diseases is not only feasible but also satisfying, it requires thorough preparation and attention to the particular difficulties that are linked with each kind of cancer. In order to improve the effectiveness of

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treatment, it is advised that neurophysiological tracking be performed whenever it is not impossible to do so.

Conflict of interest:

The authors declare that they have no conflict of interest.

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