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A Case Report of Intraspinal Neuroendocrinoma and Literature Review

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Abstract: Neuroendocrine tumor (NET) is a group of heterogeneous tumors originating in the diffuse neuroendocrine system [1,2]. It can be found in various parts of the body, but is most often found in the digestive tract and the bronchus. Primary NET in the spinal canal is extremely rare. In May 2019, our department admitted one patient with primary intraspinal NET, and the report is as follows.

Keywords: Intraspinal Neuroendocrinoma; Literature Review

The patient, whose last name is Shi, is a 74-year-old male. He was admitted to our department in May 2019 due to "low back pain with numbness in the right lower limb for half a year". The patient began to have low back pain half a year ago, which was accompanied by tingling and discomfort in the right lower extremity, numbness in the lateral upper right calf, and intermittent claudication. He received symptomatic treatment with non-steroidal drugs, but the effect was poor. In the course of the disease, the patient two normal, no low heat night sweat emaciation. According to the physical examination, he had no deformity in the spine, his lumbar mobility was acceptable, lower lumbar right knocking pain was accompanied by obvious right lower limb radiation, right lower leg lateral hypoesthesia, muscle strength of both lower limbs was normal, muscle tension was not high, straight leg elevation was more than 60°, bilateral physiological reflex was decreased, and pathological signs were negative. The results of the Laboratory examination were as follows: CRP0.6 mg/l, white 10.2 * 10 (9), ESR5mm/h, PSA0.62 ng/ml, AFP1.94 ng/ml, CEA4.81 ng/ml, CA1998.13 ng/m. There were no obvious anomalies on the lumbar positive side（**Figure 3**） Plain CT scan showed no obvious vertebral body damage（**Figure 4**）, and MR and enhanced MR of the lumbar spine showed subdural cystic space occupying in the lumbar canal at the level of 4, and cerebrospinal fluid was unobstructed.(**Figure 1,2**）

Imaging examination (**Figure 1,2**) MRI showed subdural extramedullary space occupation in spinal canal of L4 level

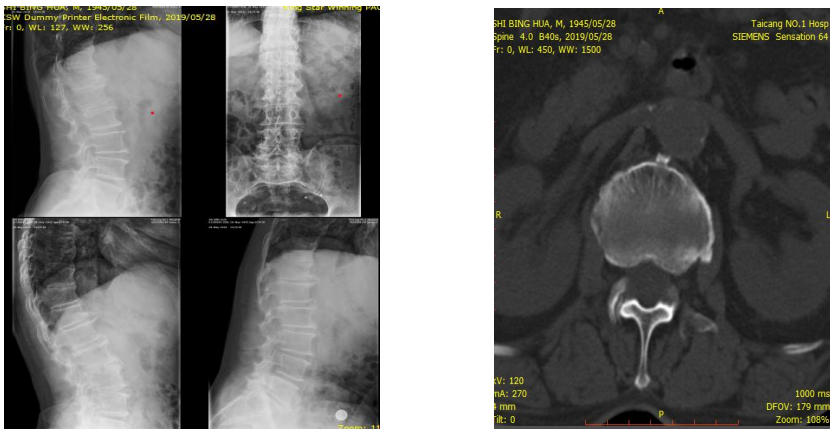

Figure 2. No obvious spinal and canal occupying lesions or bone destruction were observed on the X - ray

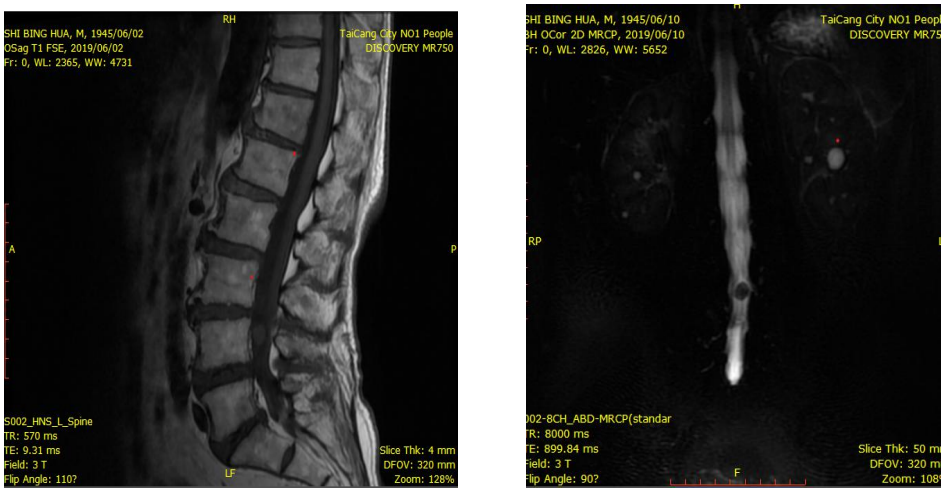

Figure 3. Plain CT scan showed no obvious space-occupying lesion or vertebral bone destruction in the spinal canal, and the signal of paravertebral soft tissue was normal

Admission diagnosis: spinal canal occupation, nature to be investigated: schwannoma?

Based on the preoperative discussion, the following diagnoses were probable: (1) schwannoma: spinal canal schwannoma is a common benign tumor, mainly originating/arising from nerve root sheath schwann cells. Its disease process is long, and accompanied by no obvious symptoms, it is common in patients with early onset, the clinical signs and symptoms are often related to the location and size of the tumor, pain is the main symptom, As the disease progresses, most patients gradually develop paresthesias and movement disorders. Intraspinal schwannomas are, in most cases, single, and often occur in the cervix and thoracic segment. It also occurs/ is also discovered less often in the lumbosacral segment, and mostly in left and right sides and posterior sides of the spinal cord. It is usually round nodules with intact capsule, accompanied by spinal cord edema and softening. Intramedullary epidural is a common growth site of intramedullary schwannoma, which usually grows along the nerve root sheath and often presents a circular shape. (2) spinal arachnoid cysts: subdural arachnoid cysts are the most common, while epidural arachnoid cysts are extremely rare. The most common place is thoracic vertebra, followed by lumbar and lumbosacral. The occurrence of epidural arachnoid cyst is related to dura rupture, whose cause can be categorized into congenital factors and acquired factors. Congenital factors are caused by dysplasia, whereas acquired factors include trauma, inflammation, and iatrogenic injury such as lumbar puncture. Clinical symptoms include limb weakness, fatigue, walking inconvenience, numbness sensory, radiculopathic pain, pain in the corresponding segments of the spine, and dystocia. The disease often presents progressive aggravation. MRI is the most important diagnostic method for epidural arachnoid cysts. Most of the arachnoid cysts are located in the dorsal side of the spinal cord. The MRI signal intensity is consistent with the cerebrospinal fluid: uniform, clear edge, low signal in T1 phase and high signal in T2 phase. There was obvious capsule or tumor wall, and the cyst could extend into the foramen and surround the nerve root, but there was no obvious enhancement in the enhanced scan.

Patient took prone position after general anesthesia: Incise at L3-L4 level. Bluntly dissected paravertebral tissue, revealing L3-L4 lamina and facet joints, then we performed bilateral pedicle screw fixation, L4 laminal decompression, make sure the canals of nerve root were enlarged. No obvious intervertebral disc herniation was observed, nerve root is loose, silk thread suspension longitudinal open the dural sac after dural sac, found in the horsetail nerve bundle class 1.2 * 1.2 * 1.0 $cm^{\wedge 2}$ round capsuled light red bump complete resection (**Figure 5**). Then we performed continuous side whipstitch for dural sac anastomosis. Installing connecting rod and nut locking before closure. Total intraoperative blood loss was 350 ml with surgery duration for 2 hours.

After surgery, the internal fixation position was good .(**Figure 8**）)

Immunopathology suggested CGA+,SYN+,CD56+, weakly positive CKP, EMA-,CK20-, ttf-1 -,NapsinA+, ki-67 (about 20%), suggesting neuroendocrine tumor of the spinal duct, G1.

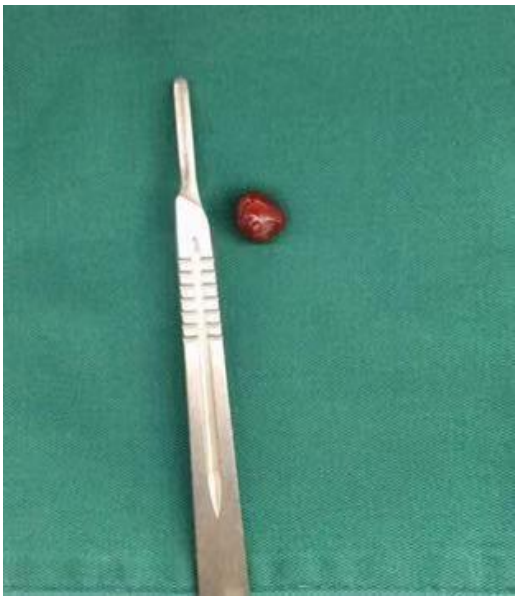

Figure 5. Intraoperative enhancing resection of 1.2*1.2*1.0 cm round capsule complete palered mass

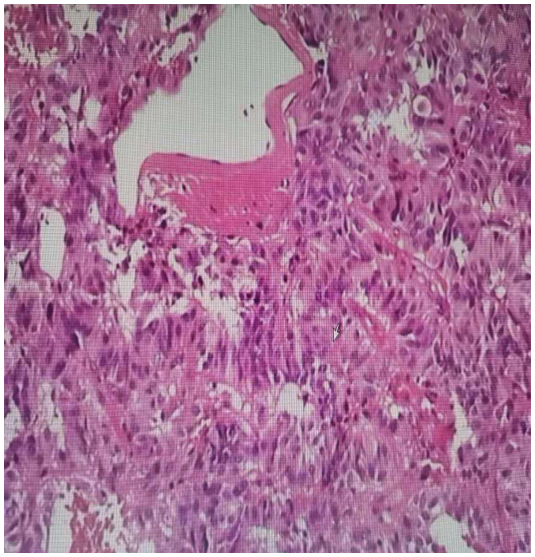

Figure 6. Pathological examination showed that the tumor cells were adenoid, papillary and diffuse patchy distribution. The tumor cells were small in size, with medium cytoplasm and red staining

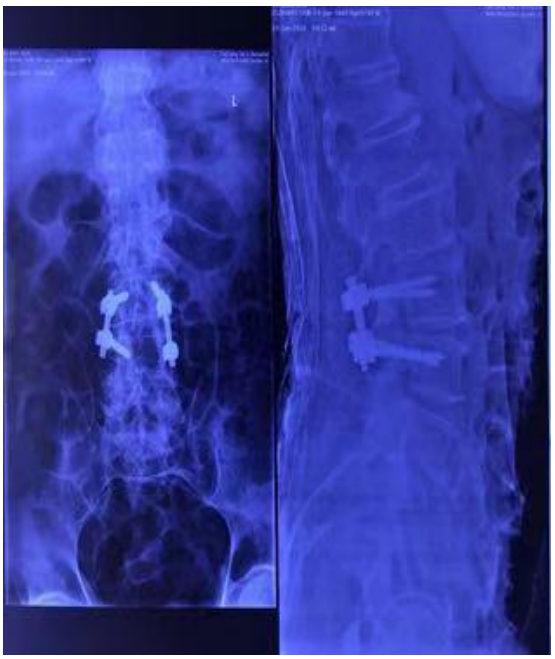

Figure 7. Postoperative X-ray showed that the internal fixation position was good

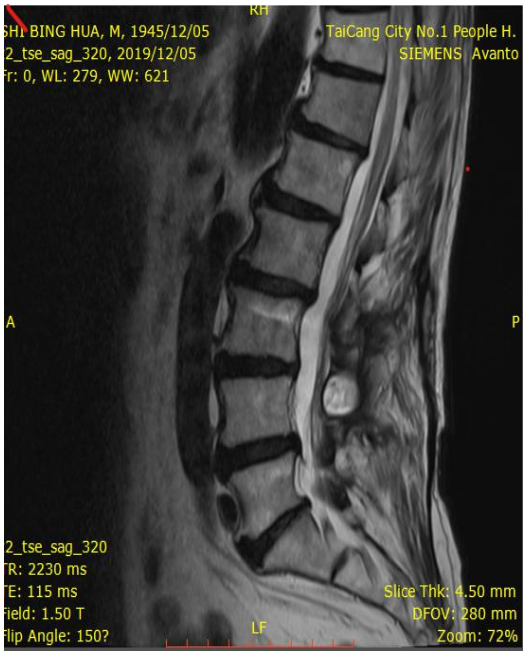

Figure 8. Six months after the surgery, MR reexamination showed no tumor recurrence

After the operation, lumbosacral pain was significantly relieved, muscle strength and sensation of both lower limbs were not abnormal, the sellar area was normal, and both stools were normal. Due to the special pathology type of the lesion, we performed a literature review. NET in the spinal canal was confirmed by postoperative pathology, so it is often necessary to complete postoperative examination to screen other organs for the presence of primary NET tumor foci or other metastatic foci. Pet-ct examination can show the location of the tumor and accurately locate it by CT. But，there was no PET-CT in our hospital，so PET-CT examination（patient ID P21973）was conducted in Suzhou Kowloon hospital，and no primary or metastatic lesions was found in other sites，therefore, so the primary ponytail neuroendocrine tumor was diagnosed. The tumor recurrence was not found in MR 6 months after operation. (**figure 6**）

Discussion

A detailed introduction of neuroendocrine tumors (NET) was first described in the literature in 1867, But over the years, the definition, naming, classification, classification, and staging of this tumor have been debated. Currently, the 2010 WHO classification criteria [3,4] are widely accepted. This criterion, combined with the classification and site-specific staging system developed by the European society of neuroendocrine oncology (ENETS) in 2007, is of great significance to the definition, naming, classification, classification and staging of the particular NET.

1. Common sites of neuroendocrine tumors:

Neuroendocrine tumors can occur in various parts of the body, but are relatively common in endocrine system, such as pituitary and adrenal glands. Neuroendocrine tumors of non-endocrine organs are relatively common in the lungs, gastrointestinal tract and pancreas, but rare in the central nervous system, especially in the spinal canal[5,6]l. Literature reports that intraspinal NET is mostly derived from NET metastasis to other parts, and metastatic intraspinal NET tends to occur in epidural, and subdural and intramedullary metastasis is rare[5,6]. Tsimpas [7] et al. believed that no more than 5% of metastatic intraspinal NET occurred under the dura. This case is low-grade malignant NET in the spinal canal. It occurred in the cauda equina nerve, and no other systemic tumor lesions were found on the pet-CT examination. So, we think this case is primary cauda equina NET.

2. The pathogenesis of intraspinal tumors:

APUD cells may originate from the neural crest, and then migrate outward from the neural crest, forming the mass neuroendocrine system of the whole body. APUD cells originating from the neural crest may remain in the spinal canal during migration, and then gradually form neuroendocrine tumors during development.

3. Clinical manifestations:

Clinical manifestations mainly include the following two aspects: (1) symptoms and signs of spinal canal tumors; (2) carcinoid syndrome. Symptoms and signs of intraspinal NET were nonspecific. Common symptoms include pain, numbness, limb weakness, and sphincter dysfunction. If accompanied by spinal damage, they may produce local lumps, and even affect the stability of the vertebral body. But the carcinoid syndrome is the tumor secreted peptide or amine hormone, the nerve medium or the neuropeptide, the manifestations include: - facial flush, - nausea, - vomiting, - diarrhea, - asthma, -heart symptom, - blood pressure fluctuation--, pigmentation and so on [8].

Diagnosis of intraspinal neuroendocrinoma

4.1 Imaging examination:

Imaging examination plays an important role in the diagnosis of NET in spinal canal. MRI plain scan + enhancement was preferred, but there was no specificity in intraspinal NET MRI. After reviewing the literature, it was found that pet-ct could exclude NET with poor differentiation and rapid tumor growth, but NET in the spinal canal was often inert and easy to be missed. In addition, somatostatin receptor-mediated radionuclide imaging (SRS) had epochal significance for the diagnosis of NET.

4.2 Examination of endocrine function and metabolites

Through the determination of neuroendocrine tumor in blood or urine of all sorts of peptide or amine, neurotransmitter or neuropeptide and its metabolites, and auxiliary diagnosis of.net, commonly used indicators are: urine 5 hydroxy indole acetic acid, 5 hydroxytryptamine, 5 hydroxy tryptophan and catecholamine, blood thyroxine, calcitonin, histamine, dopamine and chromaffin granule eggs A[8-10].

4.3 The diagnosis of intraspinal NET depends on the pathological features of morphology and immunohistochemical staining.

Cell morphology: the cells are arranged in various patterns, such as island, nest, sheet, ribbon, column or trabecular, papillary, and some of them form a flower-ring or pseudoglandular tubular arrangement. Interlacing fibrous tissue septations and sinuses: occasional regional necrosis: regular tumor cell shape. Round, oval, or polygon, of roughly the same size. Heteromorphic polymorph: round or oval nuclei. The nuclei are mostly indistinct, granular chromatin: the cytoplasm is moderately proportioned, and the cytoplasm is granular. Most are eosinophilic and mitotic.

However, immunohistochemistry showed that CK, neuron-specific enolase (NSE), Syn and CgA were mostly positive, while glial fibrillary acidic protein (GFAP) and s-100 were mostly negative. A 67 Ki index varies according to the tumor grade, electron microscopy is in less than 2 out of 10 high vision fission like for G1, 2-20 nuclear fission as for G2, more than 20 fission like to G3, G1 and G2 is commonly referred to as a neuroendocrine tumor, and G3 called neuroendocrine carcinoma, but research showed that different grading has obvious correlation with patient prognosis.

5 Treatment and prognosis of intraspinal neuroendocrinoma

At present, no paper has systematically described the treatment of primary intraspinal NET. Combined with the treatment experience of intraspinal tumors, we believe that surgical resection is still the most important treatment at present. Even if the surgery cannot completely remove the tumor. It can also reduce postoperative tumor load and provide favorable conditions for other postoperative treatments [11] (Chemotherapy is mainly targeted at low grade or poorly differentiated NET. Currently, most chemotherapy regimens are combined with chemotherapy, but the response of NET to chemotherapy is relatively poor. There are no recommendations for net-assisted chemotherapy or neoadjuvant chemotherapy in the spinal canal [11]. Other approaches include targeted drug therapy, radiotherapy, etc.

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