Abstract: Aim to report a rare case of medulloblastoma with mandibular secondaries. Background: Medulloblastoma is an embryonal tumor, common in children. It has a high malignant potential with a propensity to spread to lymphatic organs and bone, mostly vertebrae, but mandible involvement is very rare. Case History: A 10 year old male child was diagnosed with cerebellar medulloblastoma, with spinal involvement at D5 vertebral level, in 2010, for which he was treated with near total excision followed by CSI 36 Gy, with posterior fossa boost up to 54 Gy. He received 6 cycles of cisplatin and etoposide, after which there was complete remission. After being disease free on subsequent follow up, he reported again with a swelling of the jaw in 2013, which was proved to be as secondaries from medulloblastoma. He was treated with radiotherapy to a dose of 46 Gy to the mandibular swelling. There was a partial response in the lesion. The patient was put on salvage chemotherapy then using vincristine and cyclophosphamide. Conclusion: Medulloblastoma metastasizing to the mandible is a rare event. Radiotherapy to the osseous secondary was not found to completely resolve it. However, with the use of second line chemotherapy, more successful treatment might be possible but the outcome is generally poor.

CASE REPORT:
A 10 year old boy reported to our department in 2010 with complaints of headache, vomiting, diplopia. On clinical examination he had cerebellar signs positive and bilateral papilledema. On evaluation with a CT brain, he was found to have a midline posterior fossa SOL, associated with obstructive hydrocephalus. MRI brain showed a well defined, T1 hypointense, heterogenous, nodular mass lesion measuring 4.6*4.6*3.6 mm. It involved the vermis and caused obliteration of the 4th ventricle, posterior fossa basal cisterns, and caused mild tonsillar herniation. All these features were found to be suggestive of medulloblastoma, which was further proved by the post operative histopathological examination. Since medulloblastoma has a propensity for CSF (cerebrospinal fluid) spread, a spinal MRI is inevitable. This patient showed involvement of D5 vertebra on evaluation. There was no other evidence of CSF spread or any other distant dissemination on imagings. He underwent right VP shunting procedure, followed by a midline suboccipital craniotomy with near total excision of the tumor. Four weeks following surgery, he received craniospinal irradiation. A total dose of 36 Gy was given to the spine, and 45 Gy was given to the spine metastasis, followed by a boost to the posterior fossa up to 54 Gy, in 2 Gy per fraction, five days a week. Six cycles of cisplatin 50 mg in three divided doses, plus etoposide 100 mg were completed. Following this patient was on regular follow up and was disease free. In, 2013, he developed a painless swelling on the right side of the jaw, measuring 8 by 10 cm clinically. CT scan showed an osteosclerotic lesion involving right ramus of the mandible. Fine needle aspiration cytology showed small round cells, suggestive of metastasis from medulloblastoma. There were no other secondaries in the body. MRI brain and spine did not show any lesion. The policy of management was decided to be radiotherapy to the mandible secondary with salvage chemotherapy. Patient received 46 Gy RT in the fractionation of 2 Gy each for five days a week. Following radiation, the lesion showed a partial response. The patient was started on salvage chemotherapy with vincristine and cyclophosphamide following radiation. After completion of first cycle there was minimal regression in size of the lesion post RT, followed by no further decrease.
DISCUSSION:
Medulloblastoma is an aggressive tumor of the central nervous system (CNS) and accounts for 15-20% of CNS tumors in children. It is an embryonal tumor of malignant nature associated with 30-40% leptomeningeal spread at diagnosis. However, frank metastasis is uncommon at presentation. Incidence of extracranial metastasis in medulloblastoma is around 7-10 percent. In a literature review bone involvement incidence was 77% in adults and 78% in children. There are limited reports of mandible involvement, with only one case reported from India3.

The mechanism of spread of medulloblastoma was first described as leptomeningeal by Nelson. Mostly brain tumors do not spread to extracranial structures, especially before surgical intervention. The primary factors responsible for this are the short postoperative lifespan of these patients, which does not allow development or manifestation of metastasis, absence of lymphatics in the CNS; occlusion of venous channels due to compression by the tumor and immune response to the tumor cells.4 Nevertheless, it has been shown experimentally that primary brain tumour cells can keep on growing outside the central nervous system. After surgery the opening of vascular channels opens the pathway of spread.5

As this case presented with stage M4 disease (Chang Staging) at diagnosis, it was treated as a high risk1 with adjuvant chemotherapy. Recurrent medulloblastoma is an incurable and lethal disease. Although it is responsive to a variety of chemotherapy agents, durability of response is limited.6 According to a COG study, there is a significant role of cyclophosphamide, Adriamycin, and vincristine-based chemotherapy regimen. An aggressive systemic approach is needed in such cases along with radiation. Recent literature shows improved overall and event-free survival when high dose chemotherapy is followed by peripheral stem cell transplant.7

A complete surgery is the most important factor in improving the overall survival and progression free survival. In this case though the child had a complete response after craniospinal irradiation, he relapsed in the mandible, which is very unusual. The causes responsible could be microscopic disease spread through the vasculature, and the child being alive for more than two years after treatment. The prognosis however now remains poor.

Early diagnosis of medulloblastoma followed by prompt radiotherapy can result in cure. Due to lack of awareness about symptoms, and delayed medical attention most cases present in advanced stage, hence cure rates are low. Spinal metastatic disease has been shown to respond very well to chemoradiation. Also with improved methods of radiation delivery and potent chemotherapy agents the overall survival has improved. Considering these factors, a strict follow up should be maintained so as to detect any disease relapse or recurrence early. We should also look into ways of identifying cases who are more likely to develop metastasis, like DNA analysis and study of molecular factors should be encouraged[7-9]. In this way such cases can be managed up front in a more aggressive manner, as the outcome of a relapse later is dismal. Phase three trials are awaited to prove the role of newer chemotherapy regimens in the management of high-risk medulloblastoma, especially with distant metastases. The case reported here is an example of improved survival but rare relapse, which should be considered as a possibility in such cases, and prompt the treating physician to venture into more aggressive avenues of management.

REFERENCES: