INTRODUCTION

Pineoblastoma are rare malignant embryonal tumors that arise from the pineal parenchyma. These tumors are considered primary neuroectodermal tumors (PNETs) of the pineal region and exhibit aggressive clinical behavior with frequent metastases throughout the craniospinal axis [1,2].

Patients often present with findings of elevated intracranial pressure and focal neurological deficits. However, these findings are also seen in many intracranial pathologies and one of the most important is central nervous system infection. We report the case of an adult patient with pineoblastoma who presented with signs and symptoms of central nervous system infection.

CASE REPORT

A 29-year-old woman without any significant past medical history was admitted to an outside hospital with a 3-month history of headache; gait and balance disorders in September 2010. On magnetic resonance imaging; there was a 30x30x32 mm lobulated lesion with solid and cystic components. The patient was transferred to our institution. The patient underwent subtotal excision of the pineal tumor. The tumor was composed of highly cellular primitive appearing cells with narrow cytoplasm and hyperchromatic nuclei. Focal rosette formation of tumor cells was observed (Figure 1, 2, 3). Immunohistochemically; the tumor cells showed diffuse positive staining for neuron specific enolase and synaptophysin; and high proliferative labeling with Ki67 (Figure 4, 5, 6). The patient yielded a diagnosis of a pineoblastoma. Postoperatively; the patient received craniospinal external beam radiotherapy (3420 cGy) that was delivered in 11 fractions. Outpatient follow-up with laboratory and radiologic studies was performed at regular intervals. There had been no evidence of tumor recurrence for 27 months. In February 2013; she was admitted to the emergency room with fever; headache; diplopia and a feeling of numbness in the legs and hands. On her physical examination; stiff neck; severe headache and high fever (39°C) were revealed. Kernig’s and Brudzinski’s signs were positive. On her blood biochemistry; liver and kidney function tests were normal. White blood cell was 12000/mm³; and C-reactive protein was 26 IU/mL. No pathological finding was observed on her cranial computed tomography scan. A lumbar puncture was performed to diagnose acute meningitis; thus rapid diagnosis of bacterial meningitis is essential because early antibiotic therapy may reverse the patient’s severe clinical course. Protein level was found to be high (127 mg/dL); and chlorine level was normal.
in the cerebrospinal fluid (CSF) sample. CSF and blood glucose levels were 17 mg/dl and 115 mg/dl respectively (CSF: plasma glucose ratio was <0.4). White blood cell count was 250/mm³ in CSF with a predominance of neutrophils (PMNs). There were no microorganisms on Gram staining and acid-fast staining. CSF samples were inoculated to an automated blood culture system; sheep blood agar; and EMB agar. CSF cytology was also negative for malignancy. On the basis of the patient’s history and CSF laboratory findings; a central nervous system infection was not ruled out; and meropenem one gram three times a day was started empirically. Whole spinal MRI and MR venography was normal. Cranial MR showed bilateral mastoiditis; thus meropenem therapy was continued. No improvement was seen in the patient’s condition on day 23 of the antibiotic treatment. Lumbar puncture was repeated for accurate diagnosis. CSF pressure was normal and similar biochemical findings were obtained. Blood and CSF cultures and polymerase chain reaction test for Mycobacterium tuberculosis and brucella strains were negative. No pathology was detected upon cytologic examination. The adenosine deaminase activity in cerebrospinal fluid was negative. Brucella agglutination test; VDRL and TPHA tests for syphilis were negative. No acid-fast bacilli were seen through microscopic examination and Tuberculin skin test was negative; but Quantiferon blood test was positive. Anti-tuberculosis therapy with isoniazid; rifampicin; pyrazinamide and ethambutol was started.
The patient still had intermittent fever and meningeal irritation signs on the 14th day of antituberculosis treatment. A third lumbar puncture was done. Cytologic examination of CSF revealed malignant cells consistent with primitive embryonal tumor. To demonstrate the recurrence of the tumor; spinal MRI was repeated and leptomeningeal infiltration was detected (Figure 7). Antituberculosis therapy was discontinued on day 35 of the treatment. Though TB culture resulted negative; regarding KT-induced immune suppression; the patient received isoniazid alone for prophylaxis. The patient was transferred to the Oncology Department of our hospital. She was started on intrathecal treatment with 12.5 mg dose of methotrexate. Five cycles of intrathecal methotrexate failed to clear CSF of malignant primitive embryonal tumor cells and was complicated with grade 3 mucositis. Afterwards the patient’s treatment plan was changed. Two cycles of chemotherapy consisted of cisplatin (60 mg/m² once a day for the first day of the regimen); vincristine (2 mg once a day for the 2nd, 8th and 15th days of the regimen) and cyclophosphamide with mesna (1000 mg/m² once a day for the 22nd and 23rd days of the regimen) administered between May to June 2013. After 2 cycles of intravenous chemotherapy; spinal MRI was performed and pathological contrast enhancement between the arachnoid spaces was decreased. However; the patient became clinically worse and focal neurological deficit developed suddenly. The patient died on 29 August 2013; 7 months after the recurrence.

**DISCUSSION**

Pineal tumors account for less than 1% of all primary central nervous system neoplasm in adults and 3% to 8% of brain tumors in children. Germ cell tumors are the most common pineal tumors (35%); followed by pineal parenchymal tumors (PPT) (30%). Other rare pineal region tumors are astrocytomas and ependymomas[3]. Pineal parenchymal tumors consist of 3 subgroups; pineocytoma (WHO grade 1); PPTs of intermediate differentiation (WHO grade 2/3) and pineoblastoma (WHO grade 4). Pineoblastoma is classified as a malignant supratentorial PNET with a propensity to disseminate along the neuraxis and relapse [4]. Leptomeningeal metastasis (LM) constitutes the formation of secondary tumors within the leptomeninges by the seeding of malignant cells through the subarachnoid space [5,6]. Patients with LM and bacterial meningitis may have similar clinical presentation such as fever; headache; neck stiffness and vomiting. Cerebrospinal fluid (CSF) examination and MRI of the neurocranium and spine before and after contrast administration is used to obtain diagnosis; however in this case spinal seeding as the patient’s diagnosis could not be achieved though repeated Lumbar punctures and MR imaging studies were performed.

Standard treatment for LM of PB is radiotherapy followed by intrathecal chemotherapy. Our patient had received the total dose of radiotherapy for initial treatment of PB previously; thus an additional RT dose was not approved. Chemotherapy regimens show variability among centers but usually include 2 to 3 agents selected from vincristine; cisplatin/carboplatin; cyclophosphamide; etoposide and lomustine (CCNU)[7,8]. Our patient received intrathecal methotrexate followed by intravenous chemotherapy including cisplatin; vincristine and cyclophosphamide.

The outcome for patients with pineoblastoma is poor. Dissemination; poorly differentiated carcinoma; and residual disease after initial treatment were reported as independent risk factors associated with poor median overall survival [9]. Standard of care includes maximal surgical resection with adjuvant craniospinal irradiation and systemic chemotherapy; resulting in a median survival of 16 to 20 months and a 5-year survival rate of 10% [10,11]. Our patient - 29 years old at diagnosis - lived 35 months.

In a patient who presents with fever and findings of the central nervous system; first of all; infection of the central nervous system should be considered; and empirical antibiotic treatment should be started before the diagnosis is definitive. However; CSF findings do not always guide us sufficiently; and in some cases; they even prolong the time to diagnosis of the actual underlying disease.

Tuberculosis has a special place among CNS infections. Although molecular tests are also used for diagnosis today; it is still difficult to diagnose tuberculosis. Our country is in a geography where the incidence of tuberculosis is high. Therefore; BCG vaccination of the newborn is routine. BCG vaccination administered in childhood causes positivity in the tuberculin skin test.
test (TST); which makes it unclear whether the TST positivity in an adult is because of the vaccine or infection. The quantiferon test is not affected by the BCG vaccine administered in the past; but positivity is observed only in case of actual infection. In these cases; a quantiferon test performed on serum helps to distinguish between actual infection and TST positivity due to BCG vaccine. If the TST is negative and the quantiferon test is positive in a person; it indicates that the person is most probably infected with tuberculosis. However; the test cannot tell if the disease is active or inactive. For this reason; as we could not diagnose any other disease till then either; we had to consider the quantiferon test meaningful; and we started the anti-tuberculosis treatment.

However; the disease did not respond to anti-tuberculous therapy and mycobacterium tuberculosis could not be isolated in CSF. Cytologic examination of cerebrospinal fluid was positive for malignant primitive embryonal tumor cells with repeated sampling of CSF.

In conclusion; PBL is an aggressive tumor that has a tendency to metastasize along neuraxis and also recur locally[12]. Months after tumor resection; the patient may present with the symptoms of meningeal irritation and indiscernible clinical presentation of other causes of meningeal inflammation.

ACKNOWLEDGEMENTS

Authors had no additional financial support or national funding for this study.

None of the authors has any proprietary interests or conflicts of interest related to this submission.

This submission has not been published anywhere previously and that it is not simultaneously being considered for any other publication.

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