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H1N1 Infection in children with Hematological Malignancies

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In the recent pandemic of H1N1 infection, pediatric patients with haematological malignancies were considered high risk for severe illness. There is paucity of data regarding course of H1N1 infection in this subgroup. We describe H1N1 infection in 3 children with acute leukemia. All three patients presented with neutropenic fever; 2 had probable fungal pneumonia based on chest imaging and galactomanan estimation. Diagnosis of H1N1 infection was delayed in all 3 patients as it was not suspected initially. One patient died despite treatment. H1N1 infection may coexist with other infections in febrile neutropenia.

Key words : H1N1 infection, Hematological malignancies, Pneumonia.

Risk factors for severe illness and death due to H1N1 infection include young children, obesity, chronic lung disease, pregnancy, heart disease, neurocognitive disorders and immunosuppression [1]. In India, till now there have been 31866 confirmed cases and 1517 deaths of lab confirmed cases [2]. We describe the diagnostic challenges, course and outcome of H1N1 infection in three children with different hematological malignancies.

CASE REPORT

We had three patients with different haematological malignancies in varied phases of treatment who were found to have H1N1 infection between December 2009 and March 2010. The clinical details are shown in **Table I**. Diagnosis of H1N1 infection was based on quantitative polymerase chain reaction from nasopharyngeal swabs. Chest radiological findings mimicked invasive aspergillosis in two patients. Galactomanan assay was also supporting fungal infection in these patients thereby suggesting a diagnosis of probable invasive aspergillosis. Bronchoalveolar lavage could be performed in only one patient (patient 3) who grew *Pseudomonas* species in the lavage fluid. All children were neutropenic at the onset of symptoms. One patient (patient 1) died due to respiratory

failure and shock. In this patient, there was a delay of more than 10 days to initiate treatment with oseltamivir, H1N1 infection was not suspected initially. The diagnosis and treatment of H1N1 infection was delayed in patient 3 also, but he improved with treatment as his disease was in remission and total leucocyte counts and neutrophil counts were showing on improving trend.

DISCUSSION

It is interesting to study the course of this infection during the recent pandemic in this subgroup of patients as pediatric age group and malignancies both are considered to be risk factors for severe illness due to this infection. Patients with hematological malignancies are expected to have more morbidity and mortality due to the already compromised immunity, associated neutropenia, and coexistent bacterial and fungal infections. Usually a diagnosis of bacterial infection is considered in the setting of neutropenic fever and thereafter a fungal infection is considered if fever persists. It is for this reason that the diagnosis of H1N1 infection was not considered initially in our patients. The diagnosis was further delayed due to the radiological features being suggestive of invasive fungal infection in two patients. It is possible that H1N1 could have been a coexistent infection with other usual infections

TABLE I CHILDREN WITH H1N1 INFECTION AND LEUKEMIA

Parameter	Patient 1	Patient 2	Patient 3
Age/Sex	17 year/male	7 year/female	14 year/male
Underlying diagnosis	AML	Pre B ALL	Pre B ALL
Disease status	active disease	remission	Remission
Phase of treatment	day of onset of induction with daunorubicin and cytosine arabinoside (3+7 regimen)	maintenance therapy with 6-mercaptopurine and methotrexate D+31	day 27 of reinduction protocol of ALL comprising pre-dnisone, vincristine, daunorubicin and L-asparaginase
WBC/ANC (X10 ⁹ /L)	8.5/0.6	0.2/0	1.7/1.0
Clinical features	high grade fever, dry cough, dyspnea	high grade fever, dry cough and dyspnea	dry cough and high grade fever
Radiological findings (HRCT Chest)	bilateral multiple nodular patchy consolidation with ground glass opacities.	HRCT chest not done as radiograph was normal.	areas of confluent consolidation in left upper lobe along with ground glass haziness and consolidation in superior segment of left lower lobe
Galactomanan assay, (positive OD index >0.5)	Positive	not done	positive
Treatment apart from oseltamivir	piperacillin-tazobactam, imipenem, vancomycin, amphotericin B, voriconazole	cefoperazone-sulbactam, amikacin, vancomycin, amphotericin B	imipenem, amikacin, vancomycin, amphotericin B, voriconazole
Duration between presentation and diagnosis of H1N1	12 days	4 days	15 days
Duration of oseltamivir	2 days	5 days	5 days
Dose of oseltamivir	75 mg BD	75 mg OD	75 mg BD
Response to oseltamivir	no improvement	improved	no improvement
Final outcome	Died	improved	improved with continued antibiotics & antifungals

AML – acute myeloid leukemia; ALL – acute lymphoblastic leukemia; WBC – white blood cell count; ANC – absolute neutrophil count; HRCT – high resolution CT; OD index – optical density index.

seen in our patients rather than isolated H1N1 infection. Interestingly, bacterial co-infections have been previously observed in lung tissues of 29% of fatal cases of H1N1 [3].

There is paucity of data on the course and outcome of this novel infection in patients with haematological malignancies [4-7]. Sidi, *et al.* [7] found in their series of 45 patients of different malignancies that H1N1 was more common in hematological malignancies than solid tumors; however, it was not associated with severe illness or death in any of their patients. There is no published data so far about this infection in pediatric patients with hematological malignancies.

In view of our findings, we suggest that in the setting of hematological malignancies, H1N1 infection should be considered and tested by PCR in all such children, with cough or upper respiratory symptoms during an epidemic; whether the patient is neutropenic or not, and even when radiology is suggestive of classical bacterial or fungal pneumonia. Further, empiric treatment with oseltamivir should be initiated early in these patients as this infection appears to have an adverse outcome either due to its own

course or by having an additive effect on an underlying coexistent pulmonary infection.

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Intramedullary Spinal Cord Abscess Masquerading as Spinal Tumor

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We report a 5-year-old girl who presented with acute onset paraparesis with differential loss of sensation. Magnetic resonance imaging of spine revealed exophytic intramedullary mass lesion from T12 to L1. Peroperatively, the diagnosis was confirmed as abscess. The patient recovered following decompression and antibiotic treatment.

Key words: Dissociative anesthesia, Intramedullary abscess, Paraparesis.

Though spinal abscesses, especially acute epidural abscess or following caries spine are seen occasionally in pediatric population, intramedullary abscesses are seen very rarely [1-5]. We report a 5-year-old girl who presented as acute paraparesis without significant pyrexia or vertebral anomaly. Contrast enhanced MRI suggested a spinal cord tumor, which on surgery was detected to be an abscess.

CASE REPORT

A 5-year-old developmentally normal girl who presented with pain in lower abdomen for 7 days, followed by progressive weakness of both lower limbs and increased frequency of micturition of 5 days duration. Parents noticed decreased sensations in lower limbs. There are no history in recent past suggestive of any infections or treatment. On examination, the patient showed no spinal deformity or dermal sinus. Neurological examination revealed a cooperative child with normal higher functions. Cerebellar signs and signs of meningeal irritation were negative. Fundus exam was normal. Motor examination revealed hypotonia in lower limbs, power was 3/5 in dorsiflexion at both ankle and 4/5 in flexion and extension at both knee joints. Deep tendon reflexes were normally elicitable. Babinski reflex was bilaterally positive. There was differential loss of pain and temperature upto inguinal ligament in both lower limbs but vibration and position sense were preserved. There was no sacral anesthesia and

anal reflex was elicitable. Investigations showed normal chest and dorsolumbar spine X-rays, urinalysis and CSF examination. Mantoux test was negative and the ESR was 22 mm in first hour.

MRI spine revealed well defined circumscribed partially exophytic intramedullary mass measuring 1.7 cm at D12- L1 level, which was hypointense on T1 weighted images and hyperintense on T2 weighted images with internal hemorrhage along with long segment cord edema from C5 to L1 level. Contrast enhancement with gadolinium showed scattered enhancement mainly at periphery, suggestive of an astrocytoma or ependymoma.

Per-operatively, intramedullary abscess at D12 level was found, which was drained. Pus sent for gram and AFB staining and culture revealed no growth. Subsequently, the patient was treated with oral prednisolone, ceftriaxone, cloxacillin and amikacin for 4 weeks. The patient showed marked improvement in all symptoms within 2 weeks of surgery. At discharge, 4 weeks post surgery, the patient was ambulatory with power of 4+ in both lower limbs and return of bladder and bowel sensations. The diagnosis of primary intramedullary spinal abscess was made.

DISCUSSION

Intramedullary spinal cord abscess is rarely seen in children with only 38 reports in children [1]. It occurs more frequently in males with peak incidence in first and