H1N1 Vaccine-Related Acute Transverse Myelitis

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Influenza is a major health problem. Further data are needed to ascertain the clinical spectrum of the neurological complications of 2009 H1N1 [1]. The incidence of neurological complications after H1N1 vaccinations has not yet been fully reported. At the 2010 American Academy of Neurology meeting, Yacoub et al. [2] reported 35 cases of Guillain-Barre syndrome following vaccination, a number even lower than that following the seasonal flu vaccination. We describe a case of partial transverse myelitis that occurred a month after H1N1 vaccination.

PATIENT DESCRIPTION

A 44 year old previously healthy man was admitted to the emergency department with impaired sensation of the right leg. Over a few days he progressively developed diminished sensation on the right side of the abdomen followed a few days later by urinary urgency. The symptoms had started after 2 days of fever, and a month after he had been vaccinated against the H1N1 virus (Focetria®, Novartis). The neurological examination revealed brisk deep tendon reflexes of the right leg with an extensor plantar response. Touch and pain sensation was impaired in the right leg and the right side of the abdomen at the level of T4. Vibration sensation was normal in both legs but proprioception was impaired in the right leg.

Routine biochemical tests and complete blood cell count were normal. Results of additional laboratory work were normal or negative, including erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody titer, thyroid functions tests, anti-neutrophil cytoplasmic antibodies, alpha-fetoprotein, carcinoembryonic antigen, and complement. Cerebrospinal fluid analysis showed normal glucose and protein level, 7 white blood cells and 1 red blood cell/mm³, no pathological cells, and positive oligoclonal bands. Cerebrospinal fluid bacterial cultures were negative, as was CSF serology for West Nile virus (immunoglobulin G and M). H1N1 antibodies were detected in the serum (hemagglutination inhibition; 1:80) but were absent in the CSF.

Spinal magnetic resonance [Figure] imaging showed a normal configuration and spinal pattern of the thoracic cord, intervertebral disks and osseous structures. The cervical MRI showed a hyperintense lesion involving the cervical cord at the C6 and C7 levels with mild expansion of the cord and enhancement with gadolinium. The findings were consistent with transverse myelitis. Non-contrast head computed tomography as well as brain MRI was normal except for a large cisterna magna. The patient was treated with intravenous methylprednisolone 1 g/day for 5 days and recovered almost completely.

COMMENT

Our patient had no history of previous optic neuritis and there were no brain abnormalities suggestive of multiple

CSF = cerebrospinal fluid

Cervical magnetic resonance imaging showing a hyperintense lesion involving the cord at the C6 and C7 levels with mild expansion of the cord. [A and C] T2-weighted, [B] short tau inversion recovery.
sclerosis. There was no spinal cord compression, other neurological disease, history of irradiation or progression over 4 weeks [3]. The clinical, laboratory and imaging results are concordant with the diagnosis of acute transverse myelitis with mild pleiocytosis, the presence of positive oligoclonal bands (showing intrathecal antibody synthesis) and the gadolinium enhancement on MRI — all pointing to an inflammatory process. Those results are in accordance with the report of 41 cases of idiopathic acute transverse myelitis in Rio de Janeiro where 14/34 patients had a CSF pleiocytosis ranging from 5 to 277 cells/mm³ and 38% had positive oligoclonal bands ranging from 5 to 277 cells/mm³.

A complete etiological workup was negative. The fact that the symptoms and signs had occurred a month after the H1N1 vaccination suggests the pathogenesis of post-vaccinal myelitis due to an immunological reaction to the vaccine. The serum H1N1 antibody titers are consistent with immunization.

Transverse myelitis is rarely reported after vaccination. In a systematic review of PubMed, EMBASE and DynaMed for all English-language journals published between 1970 and 2009, Agmon Levin et al. [5] found only 37 reported cases of transverse myelitis that were associated with various vaccines given to infants, children and adults. In most of these cases the temporal association ranged from several days to 3 months [5].

While currently learning the lessons from the pandemic H1N1 virus [1], we should gather all possible information regarding the virus and its presentations, as well as the complications associated with the vaccine. The fact that our patient had received a vaccine with adjuvant might point to the role of the adjuvant in the development of an immune mediated neurological complication.

### References

### Capsule

**Duplications of the neuropeptide receptor gene VIPR2 confer significant risk for schizophrenia**

Rare copy number variants (CNVs) have a prominent role in the etiology of schizophrenia and other neuropsychiatric disorders. Vacic et al. performed a large two-stage genome-wide scan of rare CNVs and report the significant association of copy number gains at chromosome 7q36.3 with schizophrenia. Microduplications with variable breakpoints occurred within a 362 kilobase region and were detected in 29 of 8290 patients (0.35%) versus 2 of 7431 controls (0.03%) in the combined sample. All duplications overlapped or were located within 89 kilobases upstream of the vasoactive intestinal peptide receptor gene VIPR2. VIPR2 transcription and cyclic-AMP signalling were significantly increased in cultured lymphocytes from patients with microduplications of 7q36.3. These findings implicate altered vasoactive intestinal peptide signalling in the pathogenesis of schizophrenia and indicate the VPAC2 receptor as a potential target for the development of new antipsychotic drugs.

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### Capsule

**Initial genome sequencing and analysis of multiple myeloma**

Multiple myeloma is an incurable malignancy of plasma cells and its pathogenesis is poorly understood. Chapman and team report the massively parallel sequencing of 38 tumor genomes and their comparison to matched normal DNAs. Several new and unexpected oncogenic mechanisms were suggested by the pattern of somatic mutation across the data set. These include the mutation of genes involved in protein translation (seen in nearly half of the patients), genes involved in histone methylation, and genes involved in blood coagulation. In addition, a broader than anticipated role of NF-κB signalling was indicated by mutations in 11 members of the NF-κB pathway. Of potential immediate clinical relevance, activating mutations of the kinase BRAF were observed in 4% of patients, suggesting the evaluation of BRAF inhibitors in multiple myeloma clinical trials. These results indicate that cancer genome sequencing of large collections of samples will yield new insights into cancer not anticipated by existing knowledge.

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