Chapter 63

Status Migrainosus

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STATUS MIGRAINOSUS

Definition

International Headache Society (IHS) code and diagnosis: 1.5.2 Status migrainosus (9)
World Health Organization (WHO) code and diagnosis: G43.2 Status migrainosus
Short description (International Classification of Headache Disorder, Second Edition, 2004): A debilitating migraine attack lasting for more than 72 hours

Diagnostic criteria:

A. Present attack in a patient with migraine without aura is typical with previous attacks except for duration.
B. Headache has the following features:
  1. Unremitting for >72 hours
  2. Severe intensity
C. Not attributable to another disorder

A headache that is equally debilitating but lasting somewhat <72 hours may require the same considerations and treatment as reviewed here. Headaches that are nondebilitating but otherwise meet the criteria for status migrainosus may be coded as 1.6.1 Probable migraine without aura.

Clinical Features of Status Migrainosus (SM)

Migraine is a complex syndrome with symptoms in five domains (2): pain, general irritability (photophobia, phonophobia, kinesophobia, osmophobia), gastrointestinal (GI) (nausea, vomiting, diarrhea), neurologic (cortical and brain stem), and mood (psychiatric, irritability, depression, or occasionally euphoria). In SM, pain, general irritability, and GI symptoms predominate. Whether these lead to mood changes or whether short temper and depression are part of the migraine process is unclear. SM typically resembles the subject's usual severe migraine but there may be a spread of pain to other areas as the headache persists and the spread of allodynia or "secondary windup" occurs (1). The process appears to become a self-regenerating one as the patient has periods of some improvement and then worsening. The GI symptoms may become very severe. Persisting vomiting and diarrhea may lead to electrolyte imbalance, dehydration, hypotension, and even shock. Listlessness and easy fatigue may be very prominent.

Typically, photophobia, phonophobia, and kinesophobia are severe. As the headache persists the patient usually becomes increasingly irritable and the tolerance to pain diminishes. If allodynia occurs the pain continues to increase.

The differential diagnosis is that of migraine syndrome, which is reviewed in Chapter 45 by Swanson and Sakai. The most pressing entities to rule out are reviewed in Table 63-1. Unless severely dehydrated or in shock, the SM subject will have a normal neurologic examination (or no new neurologic findings) and normal mental status. Imaging by computed tomography or magnetic resonance imaging is in order if there are new neurologic findings.

Precipitating Factors

In the first report on SM (4), emotional stress, depression, medication abuse, anxiety, diet, and hormones were noted to be major triggering or adjunctive factors. Psychiatric factors of depression and anxiety continue to be major contributors producing stress, sleep loss, fatigue, and increased susceptibility to migraine. Depression is frequently seen and the patient should be carefully evaluated for this problem (4,14).

In women, hormonal status needs to be assessed. The premenstrual or perimenstrual part of the female cycle is a time of particular risk for SM. The patient should also be assessed for recent infection such as "flu syndrome," upper respiratory infection, or urinary tract infection, as these may trigger SM.

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TABLE 63-1 Differential Diagnosis of Status Migrainosus

A. Toxic exposure
1. Organic agents
   a. Organic solvents
   b. Aerosols
2. Inorganic agents
   a. Heavy metals (Pb, As, Hg, Bi, Cd)
   b. Acidosis, alkalosis
3. Fumes exposure
4. Medications that can produce headache as a toxic effect

B. Metabolic changes
1. Hypovitaminosis
2. Major organ failure—renal, hepatic, CO_2 retention, acidosis
3. Endocrine—hypothyroid, hypoadrenal

C. Infectious problems
1. Intracranial
   a. Encephalitis
   b. Meningitis
2. Extracranial
   a. Peritonsillar abscess
   b. Otitis media, mastoiditis
   c. Herpes zoster of cranial nerves

D. Inflammatory arteritis or vasculitis
1. Polyarteritis nodosa
2. Systemic lupus erythematosus
3. Isolated central nervous system granulomatous arteritis
4. Temporal arteritis in subjects over 50 years old

E. Subarachnoid hemorrhage

F. Venous sinus or cortical venous thrombosis

G. Pseudotumor cerebri (may relate to entry F)

The relation of analgesic overuse or rebound–withdrawal–type headache (RWHA) adds another degree of complexity. In two studies of SM subjects, 61 to 78% had RWHA (3,17).

The subject with RWHA uses increasing amounts of symptomatic medication, but with decreasing relief from each dose. At some point in the cycle, not taking medication can trigger SM. The longer the subject has been in the RWHA cycle, the more likely SM precipitation occurs on sudden withdrawal. This is clearly a different mechanism from other varieties of SM.

Management of SM

Status migrainosus by definition is a severe migraine that has continued for greater than 72 hours and has been refractory to usual therapies for migraine (4). Correct diagnosis is essential, and the entities outlined in Table 63-1 masquerading as SM must be ruled out. Adjunctive or precipitating factors of SM must be sought. Hormonal factors, pre- or perimenstrual status, pregnancy, miscarriage, postpartum state, recent change in birth control pills, or hormone therapy are often factors. Psychiatric aspects such as depression, anxiety, and stress due to family or business affairs may be very important. Finally, the presence of RWHA is very important.

Treatment for this condition involves: (1) medication for the headache, (2) correction of any metabolic abnormalities such as dehydration, (3) management of nausea and vomiting and, at times, diarrhea, (4) management of the general irritability, (5) management of the psychiatric aspects, and (6) recognition of hormonal aspects (4,14,17). Because the patient has had a refractory headache for greater than 72 hours and has usually had multiple therapeutic measures, hospitalization for a short period is often appropriate.

Medications

The medication regimen for the headache includes symptomatic medication for the current headache and preventative antimigraine medication to manage the self-regenerative component of SM. Acute symptomatic medications are outlined in Table 63-2. The order of presentation of these agents reflects the experience of the authors and the literature in general.

Dihydroergotamine (DHE) given intravenously is generally a very effective first step in these patients. Raskin (15) and Silberstein et al. (17) found up to 90% effectiveness in reducing the headache to "mild" or better for the first episode of SM. In our experience (J.C.) intravenous DHE was effective 70 to 80% of the time. There are little data on subsequent episodes of SM.

The dose of DHE may vary from 0.25 to 1.0 mg q8 hourly. A dopamine antagonist such as metoclopramide may not only diminish nausea, but may also help the headache. Table 63-2 outlines a protocol for intermittent use of DHE. A protocol for continuous infusion of DHE has been published (6). Those patients who responded well to the first dose usually do better over the hospitalization than the mediocre or nonresponders. If the SM has not been broken in 48 to 72 hours, then the likelihood of good response to DHE is low.

Patients who are in RWHA due to ergotamine or triptan overuse often do very well with DHE. Those with RWHA due to minor narcotics often are more difficult and respond less well. Patients who tolerated DHE well in the hospital can be sent home with use of intramuscular or subcutaneous DHE, 1 mg IM q12 hours with relative safety over the next 1 to 2 weeks, but follow-up is required.

The other major nonopiate options are dopamine antagonists (prochlorperazine, droperidol, Thorazine, metoclopramide), intravenous lidocaine, intravenous valproate, or magnesium. Sumatriptan and naratriptan have proven useful in SM not related to RWHA due to triptans (7). If there is suspicion of triptan-related RWHA, then use of any other triptan may compound the problem and sustain RWHA. The use of these is outlined in Table 63-2.

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TABLE 63-2 Medications for Status Migrainosus

A. Intravenous dihydroergotamine (DHE)
1. Method (adapted from Raskin)
   a. Metoclopramide 10 mg IV over 60 seconds
   b. Wait 5 minutes.
   c. DHE 0.25–0.5 mg IV
   d. Wait 5 minutes.
   e. Repeat DHE 0.25–0.5 mg IV.
2. May be repeated q8 hours for 3–5 days
   a. Use a set schedule for 24 hours and then let the patient request the dose q8 hours prn.
3. Adverse effects (AEs): nausea, burning sensations, muscle cramps, vomiting, increased blood pressure, chest tightness, increased headache, and diarrhea. Do not use in patients with cardiac disease because this could exacerbate or cause myocardial ischemia
4. After 5 days the AEs begin to occur quite frequently
5. Effectiveness—70–90% of patients markedly improved

B. Intravenous sodium valproate (VPA) (5)
1. Variable rate of administration up to 500 mg/hr or 750–1000 mg in 24 hours
2. Repeat dose unclear. Keep VPA blood level below 100 μg/mL.
3. AEs: nausea, dizziness, drowsiness, increased headache
4. Effectiveness—70%

C. Intravenous droperidol (18)
1. Method
   a. 1 mg droperidol IV over 60 seconds
   b. 2.5 mg droperidol IV over 60 seconds
2. Repeat: in one study, 2.5 mg IV q30 minutes for 3 doses
3. AEs: sedation, akathisia, anxiety, severe depression shortly after injection, malaise
4. Effectiveness—70–90%, one study of 25 subjects with SM

D. Other dopamine antagonists
1. Chlorpromazine (12)
2. Prochlorperazine (11)
3. Metoclopramide

E. Intravenous lidocaine (10)
1. Method
   a. Bolus of 1 mg/kg
   b. Infusion of 2 mg/mic over 48 hours
2. AEs: hypotension, arrhythmia, hyperkalemia, central nervous system: agitation, seizures, chest pain, nausea
3. Results: variable in case reports

F. Triptans—where ergotamine or a triptan is not producing RWHA (7)

G. Steroids—mentioned but results not quantitated

H. Narcotics—may be used with great caution to try to break the pain cycle

Preventative Medications and Adjunctive Factors

The problem of headache recurrence is a major one in the SM patient. Combining the acute symptomatic therapy with a preventative antimigraine medication is often useful in preventing early recurrence of headache and enhancing response to symptomatic medications. Use of tricyclic antidepressants such as amitriptyline or doxepin in doses of 50 to 200 mg/day (3) often is helpful because these agents also have analgesic, antinauseant, and soporific properties that help in the SM therapy. Intravenous valproate up to 1000 mg/day may be useful here. Patients often tolerate relatively large doses of preventative medications in the first 4 to 7 days and then the dose may need reduction. Beta-blockers should be avoided if the patient is depressed, a frequent problem.

Psychiatric factors are very important and must be evaluated (4,14). Depression or anxiety frequently is comorbid, and brief supportive psychotherapy is an important aspect of therapy. In some cases the help of a psychiatrist may be needed.

Removing the patient from a stressful home or work environment may be an important part of the treatment. Often, telling the family to visit briefly and then let the patient rest may be very therapeutic.

It is critical that the hospital staff and the physicians be sympathetic and monitor the patient frequently. The regimens used may need to be changed on a daily basis or several times per day. If the patient feels neglected or feels the staff is unsympathetic, the result is often anger and worsening of the headache problem.

Conclusion

SM is a complex problem and its management is equally complex. The correct diagnosis is crucial. Management requires appropriate medication, metabolic support, psychiatric support, rest, and sleep. The physician usually needs to hospitalize the patient and see the patient several times per day to assess the therapy. The nonmedication aspects of treatment often become as important as those related to medication.

For the usual case hospitalization of 2 to 4 days is adequate, but there must be an outpatient follow-up regimen starting within 4 to 7 days of discharge and then tailored to the patient's need. Without this support recurrence of SM is common.

MIGRAINE AURA STATUS

1.5.3. Persistent aura without infarction (may also be referred to as migraine aura status) (9)

Diagnostic criteria:

A. The present attack in a patient with 1.2 Migraine with aura is typical of previous attacks except that one or more aura symptoms persists for >1 week

B. Not attributed to another disorder

This is a rare but well-documented syndrome. The usual reports are of two to three patients (8,13,16). The

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persistent aura has a visual component but there may be other symptoms intermittently. The patient manifests persistent visual symptoms usually similar to those experienced with prior migraine headaches. The aura symptoms may or may not begin with a migraine and then will persist for weeks to years.

Treatment has been relatively unsuccessful overall. There are reports of successful therapy with valproate (16) and acetazolamide (8). One author has seen four cases over 25 years with no treatment successful in any patient (13). In general it would appear the problem simply has to run its course.

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