Delayed diagnosis in atypical measles syndrome

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Atypical measles syndrome has been extensively documented[1-5] since the original description, by Rauh and Schmidt[6] in 1965. The syndrome is particularly likely to occur in adolescents or young adults previously vaccinated with killed vaccine and then exposed to natural infection.[7] Nevertheless, the clinical picture of atypical measles syndrome is so unlike that of typical measles that the diagnosis may be elusive unless the possibility of the syndrome is kept specifically in mind.

Case reports

Case 1

A 15-year-old schoolgirl was referred by her family physician in November 1981 for evaluation of pulmonary nodules.

She had been in good health until April 1980, when she suddenly became severely ill, with a temperature reaching 40.1°C and evidence of bilateral lung consolidation (Fig. 1). The areas of consolidation regressed, leaving pulmonary nodules (Fig. 2). The fever subsided after about 1 week, and the patient rapidly regained her normal health. No rash was observed.

Because of the chest radiograph abnormalities the patient was referred in May 1980 to a children's hospital in Quebec. Skin tests with 5 tuberculin units of purified protein derivative and histoplasmin gave negative results, and a liver–spleen scan showed no abnormality. Gastric washings showed no tubercle bacilli. Further chest radiographs showed evidence of diminution of the pulmonary nodules. It was considered that the improvement almost completely eliminated the possibility of metastatic disease. The diagnosis at the time of discharge was granulomatous disease of the lungs, probably histoplasmosis.

The patient remained well, but in October 1980 chest x-ray examination showed a possible increase in the size of the pulmonary lesions. She was admitted to another children's hospital, where detailed assessment showed no abnormality except for the radiologic findings. Comparison with the previous radiographs indicated that some of the lung nodules had regressed, and it was felt that the unidentified disease process was not active.

Because of continuing chest radiograph abnormalities and concern about the diagnosis, the patient was referred to us in November 1981. Atypical measles syndrome was considered, and inquiry at the appropriate virus laboratory revealed that the titre of antibody to measles antigen, as determined by complement fixation, in a blood sample taken in October 1980 was 1:640, significantly higher than the upper limit of the normal range, 1:80. A chest radiograph showed that several of the pulmonary nodules could no longer be identified, and the remainder were barely visible.

The patient and her mother were informed about the diagnosis of the syndrome and reassured. Direct inquiry elicited a history of measles in the patient's skating class at the time of her original illness, in April 1980. She had received attenuated live measles vaccine in March 1970.

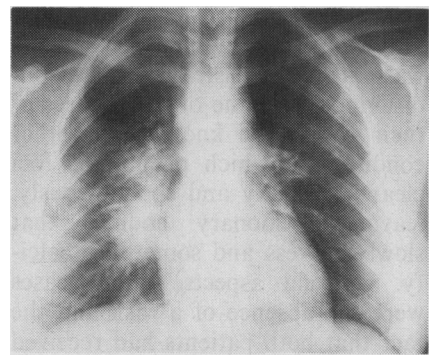

Fig. 1—Patchy areas of consolidation in right perihilar, right cardiophrenic and left axillary regions at time of acute illness in case 1.

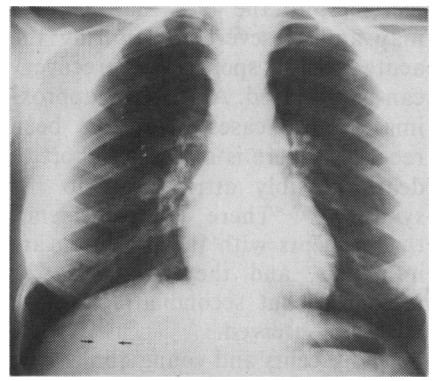

Fig. 2—Scattered nodular lesions in both lungs, best seen near right hilum and posterior to dome of right hemidiaphragm (arrows), 5 months after original illness in case 1.

Case 2

A 19-year-old man was admitted to hospital in June 1980 because of malaise, a dry hacking cough and a temperature of 39.5°C. Chest radiographs showed areas of consolida-

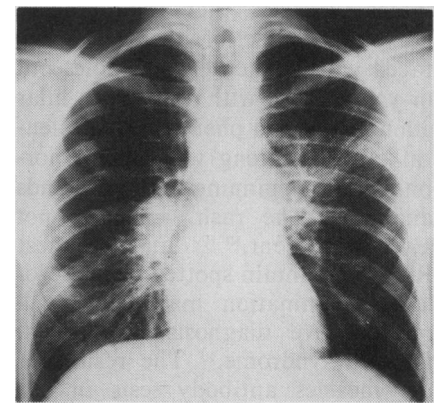

Fig. 3—Enlarged hila and patchy areas of consolidation in left upper and right lower lobes at time of admission in case 2.

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tion and bilateral hilar adenopathy (Fig. 3). No rash was seen. Diagnoses considered included bacterial pneumonia, *Mycoplasma pneumoniae* infection and acute histoplasmosis.

Treatment with erythromycin was given. The patient became afebrile within 24 hours and the radiologic abnormalities decreased. He was discharged from hospital after 1 week, having made a good recovery. All microbiologic studies gave negative results.

When the virus laboratory records were reviewed 2 years later it was noted that the titre of antibody to measles antigen, as determined by complement fixation in paired serum samples tested in parallel, had risen from 1:20 to 1:640 during the course of the acute illness. A review of his previous history indicated that the patient had received attenuated live measles vaccine together with immune globulin at the age of 3 years.

Comments

The truism that a diagnosis will not be made unless one first thinks of it is particularly applicable in atypical measles syndrome. Nichols[8] found that the syndrome was correctly diagnosed by attending physicians in only 17 of 56 patients, 42 of whom had been admitted to hospital. Knowledge of the condition through previous observation or by acquaintance with recent medical literature is a prerequisite. Textbooks may be of little help.

The entity of atypical measles syndrome is clearly defined in its own right[9] and is so different from typical measles that the clinician may not think of measles when faced with an acutely ill adolescent or young adult with high fever, hilar adenopathy and pneumonia, or pleural effusion, along with a polymorphic rash beginning on the hands and feet. The rash, which is not always present,[10-12] may suggest Rocky Mountain spotted fever; serologic examination may lead to a retrospective diagnosis of atypical measles syndrome.[13] The results of the measles antibody tests in our patients had not been appreciated, either because they were regarded as irrelevant or because they fell into the category of "data still pending"[14] when the discharge summaries were dictated or the charts were signed out. It is of interest that antibody titres greater than 1:160 are rarely observed in typical measles.[9]

A second set of problems confronts the clinician and the radiologist if the patient presents with pulmonary nodules, particularly if their relation to the initiating acute illness is not clear. The nodules, which presumably represent areas of slowly organizing pneumonia, may persist for as long as 2½ years,[3,11,15,16] during which time surgical intervention may be considered. From knowledge of the natural history of atypical measles syndrome it is clear that invasive methods of investigation, such as biopsy, are contraindicated. In one of the cases described by Mitnick and colleagues[16] exploratory thoracotomy was cancelled when a diagnosis of atypical measles syndrome was suggested by a pediatric pulmonary specialist.

The evolution of the chest radiograph abnormalities in our patients was entirely consistent with the condition, as were the other features of their cases. We know of no other condition in which pneumonic foci clear so rapidly and spontaneously, leaving pulmonary nodules that slowly regress and sometimes calcify. Unusual aspects of our cases were the absence of a rash and the fact that both patients had received live rather than killed measles virus vaccine.[2,8]

Once the diagnosis of atypical measles syndrome has been confirmed, further management is simple. Despite the fact that patients may appear severely ill during the acute illness, spontaneous recovery can be expected. Among the approximately 900 cases that have been recorded, there is only one report of death possibly attributable to the syndrome.[17] There is no evidence that patients with the condition are infectious, and they may also be reassured that second attacks have not been observed.

Adolescents and young adults who have received killed vaccine are most susceptible to the syndrome. Revaccination may be associated with adverse reactions. White[18] stated that there is no evidence that revaccination of this gradually ageing group confers protection against either measles or atypical measles syndrome. Preventing exposure to wild measles virus by means of measles elimination programs among the general population may be the most effective policy. Even if indigenous measles is eliminated in North America, however, susceptible persons will still be at risk of imported measles[19,20] and of wild measles if they travel in areas where it is still endemic.[21]

The changing epidemiology of measles has had a further, unexpected result: the firm diagnosis of measles, once the prerogative of the primary care physician, has become more elusive,[22] necessitating increased dependence on serologic tests rather than on unsupported clinical acumen.

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Visualization of *Toxoplasma gondii* in the cerebrospinal fluid of a child with a malignant astrocytoma

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In 1947 Robinson[1] described a 9-year-old girl with meningoencephalitis due to toxoplasmas so numerous as to permit ready identification on a direct smear of the cerebrospinal fluid (CSF). She recovered following sulfathiazole treatment. Feldman[2] described in 1968 a case of a child with meningitis who had *Toxoplasma gondii* in the CSF and who made a rapid, total, spontaneous recovery. We report the visualization of *T. gondii* in the CSF of a patient who was receiving immunosuppressive therapy following removal of an astrocytoma.

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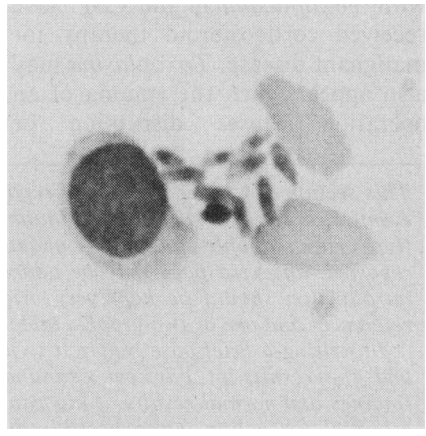

Fig. 1—*Toxoplasma gondii* visualized in cerebrospinal fluid of 12-year-old boy with malignant astrocytoma (Wright's and Giemsa; ×2150, reduced approximately 30%).

Case report

A 12-year-old boy presented with personality changes, headache, increased intracranial pressure, homonymous hemianopia and papilledema. A computed tomography scan revealing a left cerebral mass led to the diagnosis of a brain tumour. After the tumour was excised the diagnosis was confirmed histopathologically as a malignant astrocytoma of the left parietal and occipital lobes.

After the boy had been treated with corticosteroids for 14 days a sample of his CSF was taken for cytologic examination. Smears of the CSF sediment were fixed with methanol and stained with Wright's and Giemsa stains. Mononuclear cells (90% monocytes and 10% lymphocytes) and numerous organisms were found, some in the cytoplasm of the mononuclear cells. The mor-