BRIEF YALE REPORT

FEVER, SPLENOMEGALY, LYMPHOCYTOSIS AND EOSINOPHILIA: A NEW POST-CARDIOTOMY SYNDROME.

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Soon after the development of "closed" techniques for the surgical repair of acquired cardiac valvular lesions, a postoperative syndrome characterized mainly by the development of fever and pleuropericarditis was recognized in many of the patients undergoing these procedures.[1] The advent of "open" cardiac surgical procedures employing cardiopulmonary bypass has resulted in the recent recognition of another puzzling postoperative syndrome.[2,3] Some patients undergoing these procedures have developed a self-limited postoperative episode of fever, splenomegaly, lymphadenopathy, lymphocytosis and eosinophilia.

In the present report the clinical and laboratory manifestations of this new post-cardiotomy syndrome are described in three children following open-heart repair of congenital cardiac defects.

CASE REPORTS

Case 1. On 17 March 1960, R.F., a 9-year-old white male underwent open-heart surgery for repair of an interventricular septal defect. A disk-type oxygenator was used and the perfusion time was 2 hours and 1 minute. Hypothermia was not used. Preoperatively the liver was palpable 2 cc. below the right costal margin. There was no palpable splenomegaly or lymphadenopathy. The total white blood cell count was 14,000 with 31 per cent lymphocytes. Fever of 102° to 103° F. persisted during the first postoperative week and then cleared. On 7 April 1960, fever of 102° F. recurred and at the same time 10 per cent eosinophiles were present in the peripheral blood. Cultures obtained for bacterial growth were negative. Fever persisted intermittently during the next three weeks. On 21 April 1960, at the beginning of the fifth postoperative week, 50 per cent lymphocytes were present in the peripheral blood with 10 per cent of these cells resembling type I Downey cells. On 24 April, the fever had cleared and the patient was clinically asymptomatic. At this time the spleen became palpable 4 cc. below the left costal margin and discrete scattered lymphadenopathy was evident. The total white cell count was 10,100 with 75 per cent lymphocytes, 30 per cent of which were of type I and II Downey cells. Cultures for bacterial and viral studies were negative. Liver function, ASLO, C-reactive protein and sedimentation rate studies were normal. Serological studies for heterophile and toxoplasma agglutinins were negative. At the time of discharge the splenic tip was barely palpable and 50 per cent lymphocytosis persisted.

Examination six months after discharge showed that the splenomegaly, and lymphadenopathy had cleared but 50 per cent lymphocytosis persisted.

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Case 2. K.N., a 9-year-old white female, had been diagnosed as having a Tetralogy of Fallot at the age of two years. In 1953, a right end-to-side subclavian to pulmonary artery anastomosis was performed without complications. Because of the recurrence of cyanosis and retarded growth she underwent open-heart surgery on 24 May 1960 for the repair of an interventricular septal defect and the excision of an infundibular chamber below the pulmonary valve. A disk-type oxygenator was used and the perfusion time was 2 hours and 16 minutes. Hypothermia was not used. Preoperatively, the liver was palpable 2 cc. below the right costal margin but there was no palpable lymphadenopathy or splenomegaly. The total white cell count was 7,750 with 31 per cent lymphocytes and one per cent eosinophiles. Fever ranging between 101° and 102° F. was present during the first four postoperative days and then cleared. On the 26th postoperative day, fever of 101° F. was noted although the patient was clinically asymptomatic. Cultures of the blood, stool, sputum, nose and throat for bacteriological and viral studies were negative. On the following day moderate sized, non-tender posterior cervical axillary and inguinal lymph nodes were noted for the first time. The liver was palpable 4 cc. below the right costal margin and the spleen was palpable 3 cc. below the left costal margin. Laboratory data revealed a total white blood cell count of 9,050 with 72 per cent lymphocytes, 20 per cent of which were atypical and similar to type I Downey cells, and 5 per cent eosinophiles. Serological studies for heterophile and toxoplasma antibodies were negative. Liver function, ASLO, C-reactive protein and sedimentation rate studies were normal. A bone marrow examination revealed an increase in plasma cells and eosinophiles. Daily temperature spikes of 101° F. persisted for the next 10 days and then subsided. At the time of discharge on 7 July 1960, the lymphocytosis and hepatosplenomegaly persisted.

On follow-up examination one month later, the hepatosplenomegaly and lymphocytosis had disappeared.

Case 3. E.W., a 6-year-old white male, underwent open-heart surgery on 17 October 1961 for repair of an interventricular septal defect, patent foramen ovale and a tricuspid valve cleft. A disk-type oxygenator was used and perfusion time totalled 3 hours and 40 minutes. The patient was cooled to 86° F. (30° C.). Preoperatively the liver was palpable 1 cc. below the right costal margin. The total white blood cell count was 13,150 with 31 per cent lymphocytes. Fever of 101°-102° F. was present during the first three postoperative days. On 5 November he developed a fever of 101° F. but otherwise was clinically well. At this time the white blood cell count was 9,000 with 31 per cent lymphocytes, 10 per cent of which were atypical, and five per cent eosinophiles. All cultures for bacteria were negative. A low grade fever persisted during the next 18 days. On 13 November, 11 per cent eosinophiles were present in the peripheral blood. One week later the spleen was palpable 4 cc. below the left costal margin. At the same time moderate sized lymph nodes were palpated in the posterior cervical, axillary and inguinal regions. The total WBC was 8,600 with 52 per cent lymphocytes, 15 per cent of which resembled type I and II Downey cells, and seven per cent eosinophiles. On 24 November, 85 per cent lymphocytes were present in the peripheral blood. Additional studies during this period showed a normal sedimentation rate, CRP and ASLO titers. Heterophile and toxoplasma antibodies were not demonstrable.

On follow-up examination two months later the peripheral blood was normal but the splenic tip was still palpable.

DISCUSSION

The absence of chest pain, pleuritis, arthritis, and neutrophilia clearly differentiates the syndrome described from the post-commissurotomy syndrome. The pertinent features of the syndrome as exemplified by our patients was the initial development of fever and eosinophilia some time during the second or third postoperative week. In two patients this was followed shortly by the development of splenomegaly, lymphadenopathy and lymphocytosis. In the remaining patient the latter features developed two to three weeks later, after the fever had cleared. Except for the features described, all patients appeared clinically well and were asymptomatic. The course was self-limited in each case.

The pathogenesis of this new postcardiotomy syndrome is uncertain at present. Although some have suspected a viral etiology no cultural evidence to support this theory has been found.[8] Repeated cultures for bacteria and viruses were negative in our patients also. Serological studies for heterophile or toxoplasma antibodies have not been demonstrable when looked for.

Previous descriptions of similar patients have not mentioned an eosinophilia.[2,3] The presence of an eosinophilia in association with the other clinical and laboratory characteristics suggest that this syndrome may represent some form of hypersensitivity reaction. All three patients had received a variety of medications throughout their hospitalization but a careful review of the types of drugs received and the relationship of the time of original administration of each agent to the onset of the syndrome was unrevealing. It is of interest that this syndrome has been recognized following the institution of extracorporeal circulation using pump oxygenators in cardiac surgery. Two of our patients had previously undergone closed cardiac surgery with no postoperative complications. Investigation of the possible relationship between the use of such apparatus and the development of the syndrome described will be undertaken.

The incidence of this syndrome after open-heart surgery is not known. We have observed three well-documented cases among 96 patients surviving surgery during the past eighteen months. Wheeler, *et al.*[8] reported six cases among 54 patients surviving surgery in a twelve-month period while Seaman and Starr[2] described nine cases out of 250 patients undergoing open-heart surgery. A review of the records of 46 patients who underwent open-heart surgery at our hospital prior to March, 1960 disclosed an additional three patients with certain features suggestive of the syndrome. Each patient had an episode of delayed postoperative fever with an associated lymphocytosis and eosinophilia. However, no evidence of

splenomegaly or lymphadenopathy was recorded. In addition, suitable cultures and serological studies were not obtained to rule out the possibility of other underlying causes for the clinical picture.

For the present, it is important that the physician charged with the postoperative care of open-heart surgical patients be familiar with the features of this syndrome. Recognition of its onset should permit him to avoid both the unnecessary use of antibiotics and the performance of many diagnositc procedures.

SUMMARY

A syndrome characterized by fever, splenomegaly, lymphocytosis and eosinophilia was observed in three patients after open-heart surgery utilizing cardiopulmonary bypass. Its recognition and differentiation from more serious post-cardiotomy complications is important since the clinical course was benign and self-limited in all cases.

ADDENDUM

Since the submission of the present article, two additional examples of this syndrome have been seen. One is of interest in that it occurred in a 23-year-old female in whom all features of the syndrome were present except lymphadenopathy.

REFERENCES

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