ORAL MANIFESTATIONS OF AGRANULOCYTOSIS

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AGRANULOCYTOSIS is fortunately a rare condition but, nevertheless, the following three cases, all of which were seen within a period of fifteen months, illustrate the necessity of keeping it in mind when endeavouring to arrive at a diagnosis. The importance of the oral manifestations of this symptom-complex were emphasized by Mark (1934) who stated: "The frequency of the mouth lesions as the first clinical phenomenon and the rapidly fatal progress of the disease make it imperative for the dentist to be wary of treating ulcerative, non-specific lesions of the oral cavity locally, and to co-operate with the physician in ruling out the possibility of a blood dyscrasia."

CASE REPORTS

In this series all three cases were males, the first two being seen at 94th (Hamburg) British Military Hospital, and the last at the Military Hospital, York.

Case 1.—The patient, aged 20, gave a history of attending the Venereology Department where he was undergoing anti-syphilitic treatment. He was referred to the Dental Centre complaining of severe pain in his mouth. When he was examined on December 3, 1947, a large circumscribed ulcer over an inch in diameter was found on the buccal mucosa situated about the middle of the inside of the left cheek. This was surrounded by a well-defined area of petechiae, but there was no tendency towards spontaneous hemorrhage either from the ulcer or anywhere else in the mouth. The ulcer was covered by a greyish slough and there appeared to be some induration of the skin on the outside of the cheek corresponding to the situation of the ulcer. The patient also complained of a general feeling of malaise. A request was made to the Pathology Laboratory for a blood count. This revealed W.B.C. 4,400 of which only 3 per cent were neutrophils. The patient was immediately placed under the care of the medical specialist and a diagnosis of agranulocytosis was made. Constant and careful treatment of the local lesion was considered imperative as it was already serious and if allowed to spread uncontrolled it was thought it might well proceed to a noma. Again it was obviously desirable that no further drain should be put on the already grossly depleted stock of neutrophils available to combat this infection. Local applications of penicillin coupled with frequent hot saline mouthwashes were considered to be the best therapeutic agents for this means. The patient was given penicillin lozenges throughout the day while the medical specialist had already prescribed intramuscular penicillin. Subsequent blood counts were as follows:

- December 4: W.B.C. 4,300, neutrophils 2 per cent
- December 6: W.B.C. 4,300, neutrophils 6 per cent
- December 8: W.B.C. 5,500, neutrophils 15 per cent
- December 13: W.B.C. 7,100, neutrophils 35 per cent
- December 21: W.B.C. 8,000, neutrophils 57 per cent
The improvement in the blood count was accompanied by resolution of the mouth lesion. A crust formed over the ulcer which rapidly decreased in size, the petechiae disappeared and the induration of the cheek subsided. By December 21 the ulcer had healed completely.

Case 2.—This case was somewhat unusual in that the agranulocytosis occurred as a complication while the patient was undergoing treatment for a fracture of the mandible.

On July 30, 1948, the patient, aged 45, fell downstairs and sustained a bilateral fracture of the mandible. On August 4, he was operated on under endotracheal anaesthesia. As he was edentulous and the fragments of the mandible were displaced, Gunning splints were fitted to the maxillary and mandibular alveolar processes and were held there in position by circumferential and alveolar wiring. Black gutta-percha was not available for lining these splints, so tulle grass was used as a substitute. On August 21 the patient complained of malaise and had moderate pyrexia. There was also considerable pain in his mouth and throat, and extensive ulceration could be seen on the buccal mucosa. Cervical lymphadenitis was present to a marked degree. At the time it was thought that the ulceration may have been traumatic in part, due to the inefficient lining of the splints with tulle grass. In view of the malaise and pyrexia the Medical Specialist was requested to see him, and he in turn requested a blood count. This revealed W.B.C. 3,200, neutrophils 2 per cent, and a diagnosis of agranulocytosis was established. In addition to the intramuscular penicillin and pentnucleotide which the medical specialist prescribed, treatment of the mouth lesions was instituted on the lines described in Case 1. An added potential complication in this case was the risk of an osteomyelitis if the infection should spread uncontrolled along the sites of the deeply placed circumferential and alveolar wires. Fortunately, however, this did not occur. Subsequent blood counts showed a gradual improvement until on August 27 the count was W.B.C. 14,250, neutrophils 44 per cent. Again the mouth lesions had improved with the general condition. The pain had subsided, and the ulcers were almost healed. The remainder of the treatment for the fracture of the mandible was quite uneventful and, on September 14, when the Gunning splints were removed, bony union between the mandibular fragments had taken place.

Case 3.—The patient, aged 29, was referred from a nearby R.A.F. Dental Centre where he had been under treatment for gingivitis for about two weeks. An attempt had been made to extract the upper left second premolar but the tooth had fractured during the process. He was also suffering from severe conjunctivitis. When he was examined on February 8, 1949, he was pale and said he felt ill. Intra-orally there was moderate ulceration of the gingiva and he complained of pain where the tooth had been broken. Owing to this ulceration it was thought wise to defer the extraction of the premolar root for the time being, and so its surface was cauterized with phenol to attempt to alleviate the pain and local treatment for the gingivitis was commenced with penicillin lozenges. He was referred to the Eye Specialist for treatment of the conjunctivitis. By February 11, the eye condition had subsided but he now complained of severe pain from the broken tooth. As the ulceration of the gingivae had improved considerably it was thought safe to proceed with the extraction of the premolar root, and this was done under nitrous oxide anaesthesia without difficulty.

On February 15 there was a small, shallow, irregular shaped ulcer on the hard palate around which there was no evidence of inflammatory reaction. The patient also stated he had a slight spontaneous haemorrhage from his gums during the night. A request was made to the Pathology Laboratory for a blood count. This revealed W.B.C. 3,000, neutrophils 30 per cent. He was referred without delay to the medical specialist, who obtained a further history that up to two weeks previously the patient had been receiving anti-syphilitic treatment. A diagnosis of agranulocytosis was made and he was placed on intramuscular penicillin and pentnucleotide. Local treatment for the mouth was prescribed as for the previous cases. On February 17 the blood count was as follows: Haemoglobin 77 per cent, W.B.C. 1,050, neutrophils 12 per cent. Three days later the haemoglobin had dropped to 66 per cent, W.B.C. to 1,000, only 2 per cent of which were neutrophils. Also the platelet count was only 30,000. The pathologist carried out a
sternal puncture and found severe aplasia of further elements of the haemopoietic tissue. He considered the diagnosis appeared to be that of aplastic anaemia. Intra-orally the ulceration of the hard palate was static but there had been further spontaneous haemorrhages from the gingiva, and the blood clot in the recently extracted premolar socket showed no signs of organizing. The patient also complained of dysphagia and pain in the throat. Further blood counts were as follows:

February 24: Haemoglobin 56 per cent, W.B.C. 800, neutrophils 4 per cent.
February 26: Haemoglobin 53 per cent, W.B.C. 500, no neutrophils could be seen.
February 28: Haemoglobin 49 per cent, W.B.C. 300, no neutrophils. Platelets were less than 20,000.

The colour index had remained at unity in the above counts so the decrease in R.B.C. was proportionate to that of the haemoglobin.

Despite all efforts by the Medical Specialist such as transfusion and treatment with B.A.L., his general condition had gradually deteriorated and on March 1 he died. At the time of death his mouth condition was no worse than it had been a week previously.

DISCUSSION

The foregoing cases serve to show the great variation in form, severity and site of the oral manifestations which may be expected in agranulocytosis. There is nothing characteristic about these lesions except perhaps a complete lack of reaction of the surrounding tissues to infection and an absence of any local cause for the lesion. The spontaneous haemorrhages in Case 3 were merely a manifestation of the greatly decreased number of platelets and would not, of course, occur in cases of true agranulocytosis where the involvement only concerns the granulocytes. Again, the patient may be ambulatory and arrive at a Dental Centre giving little hint as to the serious underlying general condition. It is apparent that the Dental Officer is in no position to make a diagnosis from the clinical aspect of agranulocytosis as it concerns him, but his suspicions may be aroused by the presence of a non-specific ulceration in the mouth coupled with a history of recent treatment by a drug which may depress the haemopoietic function of the bone-marrow, and to which the patient may exhibit an allergy. These suspicions should be confirmed or discounted immediately by haematological examination, and if the count is abnormal steps should be taken to place the patient under the care of the Medical Specialist with the least possible delay. From current literature, examples can be provided to show that dental extractions appear to precipitate the condition and so all but the most urgent surgical intervention should be postponed.

For treatment of the general condition, penicillin therapy seems to have decreased considerably the number of cases of agranulocytosis terminating fatally. Leitner (1949) goes so far as to state "Almost all cases of acute agranulocytosis can be saved especially when treated early enough by the use of penicillin." This makes the establishment of an early diagnosis even more important than ever and, as has been shown, the dental officer is often in a position to render valuable help in this direction. Once a diagnosis has been made it is essential that, if a mouth lesion is present, however small it may be, it should be treated with the most constant and careful attention to keep it under control and to conserve the precious granulocytes. In these case reports, an attempt has been made to describe some of the varying mouth lesions of agranulocytosis and to suggest a line of local treatment for them, but
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obviously they cannot be considered as an isolated syndrome. As Appleton (1932) expresses it in a comprehensive article on agranulocytosis “The condition or conditions indicated by this term well illustrate the essential unity of Medicine.”

SUMMARY

(1) Two cases of agranulocytosis and one of the allied condition, aplastic anæmia, are reported.
(2) The varying mouth lesions of these cases are described.
(3) The importance of an early diagnosis and the possibility of the oral manifestations appearing as the first clinical sign are stressed.
(4) Prompt haematological examination and reference to a medical specialist are emphasized.
(5) The necessity of careful treatment of the mouth lesions is stated.

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