EXPERIMENTAL BIOLOGY

Metabolism of Collagen in Experimental Osteomyelitis

N. S. Strelkov, P. N. Sharaev, N. G. Naumova, and P. N. Maksimov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 127, No. 6, pp. 691-692, June, 1999
Original article submitted July 16, 1998

Serum and local bone indexes of collagen catabolism were considerably increased in rabbit pups with acute stage of tibial osteomyelitis. Chronic stage of osteomyelitis was characterized by an elevated content of hydroxyproline bound to low-molecular-weight collagen fragments.

Key Words: *osteomyelitis; collagen; hydroxyproline*

Purulent osteomyelitis is accompanied by alterations of the diploic channel tissue, while the compact bone tissue degrades later [2]. The state of organic bone matrix, primarily presented by collagen is of crucial clinical importance.

We evaluated indexes of collagen metabolism in the blood and bone tissue involved in osteomyelitis.

MATERIALS AND METHODS

Rabbit pups of both sexes weighing 1.6-2.4 kg and aging 3-4 month were used. Day-old culture of *Staphylococcus aureus* isolated from patients with pyogenic bone diseases was used as the infectious factor. A suspension (0.3 ml) containing approximately 50 mln. microbial bodies per 1 ml was injected into the upper third of the left tibia using an injection needle with a mandrin. The animals were kept under standard vivarium conditions without treatment [1].

The development of osteomyelitis was confirmed by clinical and laboratory tests and x-ray examination. During the first 5-6 days the state of experimental animals was severe. Growing edema and defense contracture appeared on days 3-5 postinjection and peaked on days 9-12. Purulent fistulas opened spontaneously. Acute inflammation decayed on days 20-30 postinjection. Transformation of acute inflammation into chronic stage with the formation of chronic fistulas was observed on days 35-40. Experiments were carried on animals with osteomyelitis and chronic fistulas.

Blood for biochemical tests was drawn from intact (control) and experimental rabbits after 5-6, 24-25, and 38-40 days. Serum contents of free (FH), peptide- (PH), and protein-bound hydroxyproline (PrH) were determined [4]. Some experimental and control animals were sacrificed on days 10-12 and others on days 38-40 of the experiment. Compact bone specimens (300-350 mg) were obtained near tibial fistula (left extremity) and in the same region of the right (normal) tibia. The specimens were cut free of soft tissues, washed with physiological saline, and homogenized [5]. Parameters of collagen metabolism were assessed as described previously [3].

RESULTS

In intact rabbit pups FH, PH, and PrH corresponded to published data [4]. These parameters sharply increased during acute osteomyelitis and returned to normal (except for PH) during chronic stage (Table 1).

The content of FH in involved bone tissue drastically increased in the acute stage (Table 2) and remained at this level during the chronic stage. The content of hydroxyproline in 2- and 16-h bone hydrolysates reflects the intensity of collagen hydrolysis and the total content of this protein in the bone tissue, respectively. Two-hour hydrolysis of intact and involved bone tissue yielded 21 and 31% hydroxyproline of its total content (released after 16-h hydrolysis).

Izhevsk State Medical Academy

0007-4888/99/0006-0631$22.00

TABLE 1. Serum Indexes of Collagen Metabolism (μmol/liter, *M±m*)

Experimental conditions		FH	PH	PrH
Control (*n*=9)		14.6±0.7	8.9±0.9	47.9±1.2
Experiment, days	5-6 (*n*=20)	38.3±3.4*	18.7±1.2*	89.4±3.8*
	10-12 (*n*=18)	26.2±3.1*	32.8±2.6*	76.7±4.3*
	24-25 (*n*=10)	24.8±2.9*	21.7±2.1*	29.6±3.4*
	38-40 (*n*=8)	16.3±1.6	19.4±2.2*	51.2±2.9

Note. Here and in Table 2: *$p<0.05$ compared with the control.

TABLE 2. Indexes of Collagen Metabolism in the Bone in Osteomyelitis (μmol/g dry tissue, *M±m*)

Experimental conditions	FH	Hydrolysis	
		hydroxyproline, 2 h	collagen, 16 h
Control (*n*=9)	2.32±0.09	42.8±1.2	204±2.9
Acute osteomyelitis (days 10-12)			
involved bone (*n*=7)	4.24±0.60*	56.7±2.9*	182±3.5*
intact bone (*n*=7)	3.01±0.21*	46.9±2.8	201±3.2
Chronic osteomyelitis (days 38-40)			
involved bone (*n*=8)	2.88±0.16*	59.3±1.9*	212±4.7
intact bone (*n*=8)	2.40±0.12	43.6±1.3	205±3.0

This accelerated collagen hydrolysis can be attributed to accumulation of low-molecular-weight hydroxyproline-containing polypeptides or collagen fragments in involved tissue.

Since the content of FH in the blood depends on the intensity of collagen degradation in the organism and the content of PH reflects intensification of collagen metabolism [1,4], collagen degradation predominates in osteomyelitis. This is confirmed by examination of the bone tissue, in particular by the total content of hydroxyproline, reflecting the total content of collagen in the bone.

Serum PrH content is determined by collagen-like proteins: 80-90% serum PrH is C1q protein, an element of the classical complement activation pathway [6], which belongs to the acute phase protein family. Accumulation of PrH in the blood in osteomyelitis can be explained by acute-phase reaction to infection.

Thus, experimental osteomyelitis is associated with collagen metabolism disturbances, especially in the inflammation focus, with predominant catabolic processes. Serum indexes of collagen metabolism reflect osteomyelitis development and can be used for prediction of course and outcome of the disease.

REFERENCES

1. V. I. Mazurov, *Biochemistry of Collagen Proteins* [in Russian], Moscow (1974).
2. K. S. Ormantaev and T. Zh. Sultanbaev, *Intraosseous Drainage in Children with Osteomyelitis* [in Russian], Leningrad (1979).
3. P. N. Sharaev, *Byull. Eksp. Biol. Med.*, **81**, No. 6, 665-666 (1976).
4. P. N. Sharaev, *Ibid.*, **101**, No. 3, 304-306 (1986).
5. P. N. Sharaev, A. I. Pantyukhin, and O. N. Zubarev, *Ibid.*, **111**, No. 4, 377-379 (1991).
6. G. A. Yarovaya and Yu. E. Ershikova, *Complement System* [in Russian], Moscow (1990).